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MECHANICAL SUPPORT OF HEALING SMALL BOWEL ANASTOMOSES BY ADHESIONS

BY

© JOHN FREDERICK ARTHUR VANCE

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled "Mechanical Support of Healing Small Bowel Anastomoses by Adhesions", submitted by John Frederick Arthur Vance in partial fulfillment of the requirements for the degree of Master of Science (Surgery).

ABSTRACT

Adhesions at the site of intestinal anastomosis are an integral portion of the total healing process. This study examines one of the mechanical functions of adhesions in both inverted and everted ileal anastomoses.

Eighty male Sprague Dawley rats, of mean weight 280 grams, had an inverted anastomosis performed 15 cm. proximal to the ileo-caecal valve. Eight rats were studied at each of the following postoperative intervals: six hours, 12 hours, 24 hours, two days, three days, four days, five days, six days, eight days and 10 days. In half the animals the adhesions were removed from the anastomosis prior to testing, and in the remaining half the adhesions were left intact. Bursting pressure studies and hydroxyproline determinations were performed on all specimens.

A similar experiment was then performed in which eighty rats had an ileal anastomosis constructed by the everted technique. Hydroxyproline determinations were not carried out in this experiment. However, bursting pressure studies and histological examinations were performed on all specimens.

In animals with inverted anastomoses, the mean bursting pressures of both groups rose from six to 12 hours postoperatively, then fell to reach a minimum at three days. Thereafter the bursting pressures rose progressively until termination of the experiment at 10 days. From day one onward, the mean bursting pressures of those anastomoses with adhesions left intact were greater than those with adhesions removed. This difference was highly significant ($p<0.05$) in the one to five day interval. During this same time interval, adhesions contributed 32%

to 68% of the total strength of the anastomosis.

Hydroxyproline concentrations in the inverted anastomoses increased from the time of operation until 24 hours postoperatively then fell, reaching their lowest level at three days postoperatively. Subsequently, they increased slowly from three to five days, more rapidly from five to six days, and fell off somewhat between six and ten days. Apart from the six day specimens, there was no significant difference in the hydroxyproline concentrations of the intact anastomoses or those from which adhesions had been removed.

In animals with everted anastomoses, the healing curves followed a similar pattern, rising from six to 12 hours, falling to a low point at two days, then rising progressively until 10 days. From 24 hours onward, the intact anastomoses were again stronger with this difference being highly significant ($p<0.05$) in the one to five day interval. In this time interval, adhesions contributed 46% to 79% of the total anastomotic strength. There was no significant histological difference in the sections apart from the presence or absence of adhesions.

In conclusion, adhesions do contribute significantly to the ability of both inverted and everted anastomoses to withstand pressure distension. Moreover, they do so at a critical time when the anastomosis itself is weakest and least able to withstand distension.

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INTRODUCTION

The mysteries of wound healing have long attracted but eluded both surgeon and scientist alike. Throughout history, knowledge of regeneration and repair has slowly accumulated, but even today, despite voluminous literature on the subject, we are only scratching the surface of truly understanding the healing process. We know the morphological sequence of wound healing and many factors retarding it, but remain almost totally ignorant of how to precisely control healing or comprehending why and how the processes of healing are initiated.

The accumulation of knowledge regarding intestinal healing differs from that of wound healing in general, only in that it developed more slowly and in lesser degree. Man concerned himself firstly with the exterior lesion that he could see, and the treatment of which left some hope for survival.

Prior to 1800, observations on intestinal healing were limited to sparse statements by a poverty of individuals. The Hindu, Susruta, described suture of the intestine in the fifth century B.C. Galen advocated animal experimentation but added little specific knowledge to intestinal healing. Albucacis, a Spanish Moslem of the eleventh century A.D., described everting closure of the intestine with ant heads. Circular suture of the intestine is mentioned by Roger of Salerno in FABRICA, and described further in the writings of his pupil, Roland of Parma.[1] Lanfrank[2] in 1396 observed that agglutination of peritoneal coats prevented effusion and contamination from the bowel, and that healing of intestinal injuries could be achieved by sewing together the visceral and parietal peritoneum. Further progress then waited four hundred years.

With the dawn of the nineteenth century, the pace of development began to quicken. The enlightened observations of a few individuals made possible not only the successful repair of traumatic injury to the intestine, but also the elective resection of bowel for the eradication or palliation of intestinal disease. With the planned infliction of injury through surgery, a more thorough knowledge of the healing process and how best to achieve it became imperative. There followed a profusion of experimental data on how the intestine heals and on which methods contribute to optimal healing. These, combined with careful patient follow-up and analysis of data from clinical studies, provide the basis for present day intestinal surgery.

Bichat[3] in 1802 noted the numerous adhesions surrounding serosa-to-serosa apposition of injured intestine. In 1812, Travers,[4] like Lanfrank, observed the healing of intestinal wounds by agglutination of peritoneal surfaces, but further recognized the importance of approximating adjacent serosal surfaces by suture. He advocated separate suture of the parietal and visceral wounds, but felt the method of suture unimportant so long as it achieved secure closure and intimate contact of the divided ends of bowel. Antoine Lembert,[5] operating at the Charité in Paris, popularized the suture which now bears his name. Of even greater importance however, was his concept, published in 1826, of inversion of wound edges with serosa-to-serosa apposition in order to achieve immediate sealing of the wound. The idea of such closure he attributed to Dupuytren, although others believe Jobert[6] to be the innovator. At any rate, the first great principle of intestinal surgery had been elucidated.

A rapid increase in the number of surgical procedures performed upon the intestine soon followed. In 1836 Dieffenbach[7] performed the first end-to-end anastomosis of the small intestine and throughout the middle and later nineteenth century, the German and Viennese schools forged ahead in this field led by Billroth, Kocher, Schimmelbusch, Czerny and Madelung. It was an American, however, who popularized the second great principle of intestinal surgery.

Although the importance of including the tough, fibrous submucosa in the suture was first described by Gross[8] in 1843, it was certainly the work of Halsted[9] in 1887 that subsequently brought international acceptance to the necessity of including this layer in the performance of anastomosis. It is the only layer of sufficient strength to allow suturing with any degree of reliability.

In the past two centuries, many methods of how best to obtain optimal intestinal healing have been published. Different suture techniques, different instruments and various modalities to render anastomosis easier and more secure, Murphy's button,[10] Abbe's catgut ring,[11] Senn's boneplate[12,13] and Halsted's inflated rubber cylinder[14] to name but a few, have all been described. Some flourished, others passed to the backwater of surgical knowledge. The nineteenth century, then, was the era of surgical technique. It was not until the late nineteenth and early twentieth centuries, however, that accurate detailed anatomic and physiologic studies were performed upon the nature of intestinal healing.

The intestine, like other tissue, reacts to injury by the process of acute inflammation. Initially, stasis and thrombosis in

vessels, exudation of fluid, intense polymorphonuclearcytosis, tissue hemorrhage, congestion and edema are predominant. This inflammatory reaction effectively seals the approximated intestinal walls with fibrin almost by the time that suturing is completed. Fellows et al.[15] demonstrated the anastomosis to be air and water tight 15 to 30 minutes following operation, and Herman et al.[16] found appreciable resistance to intraluminal distension four hours postoperatively. This initial period of inflammation is followed by a period of necrosis and sloughing of devascularized and traumatized tissue. The debris that is not sloughed is phagocytosed by polymorphonuclear leukocytes and macrophages and lysed by enzymatic activity. That this phase has a tremendous influence on the quality and rate of subsequent healing has been emphasized by Flint,[17] Herman et al.,[16] Olsen et al.[18] and others. If little devascularization, trauma and necrosis occur, the demolition phase is short and regeneration and repair supervene with rapid healing of the defect by first intention. If, on the other hand, the amount of necrosis is great, the demolition phase is prolonged and the defect left to repair is greater. Regeneration and repair then progress more slowly with the production of exuberant granulation tissue and healing by second intention. Varco,[19] Dennis[20,21] and Poth[22] have found sulfanilamides and antibiotics to be local aids to primary healing. Herman et al.[16] and others[23] find no difference in healing with or without antibiotics.

The proliferation of mucosa from the edge of the defect and from adjacent glands begins approximately two to seven days postoperatively, and mucosal coverage is usually complete in from five to 20 days,

depending upon the area of ulcerated epithelium to be covered. Initially the epithelium consists of a single layer of flattened cells, but after coverage is complete, this layer gradually becomes cuboidal and then columnar. At this stage, goblet cells begin to reappear and downgrowths of cells from the luminal layer invade the underlying tissue. From these downgrowths, the glands of the intestinal mucosa emerge about two to three weeks following operation. The appearance of crypts and villi is somewhat slower, but by thirty days the mucosa at the site of anastomosis appears essentially normal.

The healing of the deeper layers of the intestinal wall occurs essentially by fibrous union of the divided ends. Fibroblasts and capillaries invade the injured area about the third postoperative day and proliferate rapidly. Collagen is soon manufactured and aggregated causing a rapid increase in the tensile and bursting strengths at the site of repair. This increase in strength begins about the fourth or fifth day, continues maximally until ten days after injury, and then proceeds slowly for many months. Cronin, Jackson and Dunphy,[24] studying colonic anastomoses in rats, showed an initial fall in collagen levels in the first three or four postoperative days, followed by a rapid increase continuing until ten days, and followed again by a slight depression from ten to 14 days. They found this to be true of the bowel immediately above and below the anastomosis as well as the anastomotic site itself. The collagen content and bursting pressure correlated well and, after ten days, pressure distension caused rupture of the bowel elsewhere than at the site of anastomosis. Herman et al.[16] found similar data with bursting pressures, achieving normal rupturing

values at seven days, but found that linear tensile strength did not achieve normal values until 17 days. Fellows et al.[15] working with dogs, reported anastomotic bursting pressures equal to those of normal bowel at 14 days. Nelson and Anders,[25] however, pointed out the fallacy of measuring bursting pressure alone. The intestine is a cylinder, and according to the law of LaPlace, the tension exerted on the wall in a circular direction is a function of both pressure and radius and not pressure alone.

$$T \text{ circular} = PR$$

Because the anastomosis is often somewhat narrowed initially and distends less readily than adjacent bowel, the radius at this point is often less. Consequently, at equal pressures, the wall at the anastomotic site is subjected to less tension than adjacent areas. Trueblood et al.,[26] calculating bursting tensions, found that the strength of the anastomosis did not exceed that of normal bowel even at 28 days. The trend of the previous studies, however, remains valid.

Apparently no quantitative measurement of the ground substance or any of its component compounds has been done on the healing intestine, other than that of Olsen, Letwin and Williams,[18] and this study lasted only five days following wounding. These investigators demonstrated an initial marked increase in hexosamines at three days postoperatively, after which the values fell off rapidly. However, hexosamine measurements as a determination of ground substance in a bowel wound are complicated not only by serum glycoproteins, but also by the high glycoprotein content of mucous in adjacent intestinal epithelium. This would suggest that for the measurement of ground substance changes in intestinal wounds, radioactive

sulfur and/or uronic acid labelling may be the method of choice.

The muscle layers are certainly initially united by fibrous tissue, but early regeneration of the cut ends of muscle fibres is also noted. Jones[27] has shown complete regeneration of muscle following accurate apposition. This undoubtedly will occur in the intestinal muscle, given sufficient time and a minimum of intervening fibrous connective tissue through which to pass. Excessive fibrous tissue will retard the regeneration of muscle.

The subperitoneal tissue may remain thickened for a long period postoperatively. The peritoneum itself reestablishes early continuity across the site of injury; under ideal conditions, probably within the first few days.

Blood vessel regeneration also occurs early in the repair process with outsprouting of new vessels from the endothelium of the old. Capillary continuity across the anastomosis is established about nine days following injury.[28] With maturation of the anastomosis the vascularity diminishes and under ideal circumstances approaches that of adjacent normal bowel. Lymphatic and nerve fibre regeneration at the site of injury also occur.

The fate of sutures used in intestinal closure will be dealt with briefly. Catgut sutures excite a great deal of inflammatory response but are soon absorbed. Nonabsorbable sutures (silk, cotton, dacron, etc.) excite a minimum of response if they do not pierce the mucosa and enter the lumen. When they do pierce the mucosa, they are usually surrounded by considerable inflammation and, according to Reichert and Holman,[29] are soon sloughed into the lumen.

Martzloff and Suckow[30,31] also mention inclusion cysts around nonabsorbable sutures that have entered the lumen.

The above description is, however, general. With the variations in the intestinal tract, blood supply, wall thickness, consistency and contents in the lumen, prevalent disease processes, etc., variations in the healing process may also be expected.*

No discussion of intestinal healing is complete without at least passing notice to the presence of adhesions. Smith[32] noted in 1895 that "Sinister results which we seek to avoid arise when we leave raw surfaces to which intestines may adhere and cause obstruction." In 1956 Trompke and Siegner[33] noted that peritoneal injury or inflammation aroused an outpouring of fibrin which led to the formation of adhesions. Jackson[34] in 1958 concluded, however, that the majority of these fibrinous adhesions were transient and were absorbed in a few days. Nonetheless, some adhesions became fibrous and were not absorbed. Connolly and Smith[35] were convinced that peritoneal integrity was the essential factor determining the fate of adhesions. If the peritoneum was intact, the adhesions disappeared; if a peritoneal defect persisted, the adhesions became fibrous and permanent. Chandy and Rhoads[36] concluded that the rapidity of adhesion formation was a direct function of the magnitude of trauma to the peritoneum. This classical view of adhesions, then, ascribes their formation to peritoneal denudation and trauma. Contrary to these studies, however, are those of von Dembrowski,[37] Franz,[38] Robbins, Brunschwig and Foote,[39] Trimpi and Bacon[40] and Williams.[41]

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*For more complete detail on specific areas the reader is referred elsewhere.[16,17,26,30,31,52,107]

These workers demonstrated that both parietal and visceral peritoneal defects heal without adhesion formation and that the incidence of adhesions and of obstruction is, in fact, less if peritoneal defects are not closed. Ulfeder and Quinby[42] found that 50% of cases of postoperative obstruction following Miles procedures were due to incarceration of a loop of bowel between sutures inserted in an area of surgical reperitonealization. In addition, Rini and Zollinger[43] and Singleton[44] found no favorable sequelae in areas of peritoneal ulceration.

Thomas and Rhoads[45] and Ellis[46] have noted the propensity of sutures to cause adhesions. This propensity was most marked with catgut. Getzen[47] noted less adhesions with dacron sutures. Studies now underway in our laboratory suggest that although adhesions are stimulated by sutures, the leakage of intestinal content almost invariably causes adhesions in greater number and of greater density.

Ellis,[46] later supported by Myllärniemi and Karppinen,[48] has shown that adhesions may act as vascular grafts to ischemic areas of intestine. This is particularly true of the omentum. The work of Rabinovici and Fine[49] and of Belzer[50] suggests that venous stasis is a more important factor in the stimulation of adhesion formation than are lesions of the arterial circulation.

Adhesions at the site of anastomosis, then, may be stimulated by trauma, loss of peritoneal continuity, ischemia, sutures, or leakage of intestinal content. Whatever their stimulus, they occur with great frequency in regions of surgical intervention, surrounding at least initially, most areas of intestinal repair. Indeed, Ravitch and co-workers[51] illustrated the uniformly disastrous results attending all

types of intestinal anastomosis when wrapped with silastic gauze to secure isolation from the peritoneal cavity and thereby prevent the formation of adhesions.

It must also be conceded that adhesions may cover areas of primary deficiency in the repair process. In so doing, however, they preserve the life of many an organism and therefore must be considered an integral, if somewhat inconvenient, part of the total healing process.

This then is how the intestine heals. How best to achieve this ideal has long been the subject of surgical controversy. Four of the major controversies are discussed below.

A. End-to-end versus lateral (side-to-side) anastomosis

Lateral anastomoses were popular in the nineteenth century and have persisted well into the twentieth. Early surgeons, such as Connell,[53] felt them to be easier to perform as well as allowing for a greater area of serosa-to-serosa apposition and larger lumen.[54] They were therefore felt to possess a greater margin of safety. However, with increase in technical skill and experience in performing end-to-end anastomosis, it soon became apparent that "lateral anastomosis is mechanically and physiologically bad surgery" (Highsmith, 1923).[55] Cannon and Murphy[56] using bismuth contrast studies in dogs showed the ineffective peristalsis across the lumen of a lateral anastomosis (presumably due to severance of the circular muscle layer at the time of surgery), the tendency of the stoma to late cicatrical contraction, and the stasis and dilatation occurring in the blind ends of the anastomosed loops. The indications for lateral anastomosis today are few. If it must be performed, the side-end to end-side technique of

Poth[57,58,59] offers perhaps the most attractive method. Objective studies on the comparative rates of healing of lateral and end-to-end anastomoses have not been performed. Other factors being equal, it is assumed that there would be little or no significant difference.

B. Closed (aseptic) versus open anastomosis

Initially, anastomoses of the intestinal tract were performed in an open fashion. It was soon obvious, however, that opening of the intestinal tract was associated with an alarming morbidity and mortality due to sepsis, especially following procedures on the colon. Not only are the sequelae of contamination (peritonitis, intraperitoneal abscess, etc.) harmful in themselves, but they are also detrimental to the healing of the intestine. Halsted[9] noted the delayed or absent unfolding of the flange created by inverting methods,in the presence of peritoneal infection around the anastomosis. Letwin and Williams[60,61] have shown experimentally the poor anastomotic healing in the presence of peritonitis. Akpata and Curry[62] have demonstrated diminished fibroplasia and bursting strength in anastomoses infected with Escherichia coli. With contamination, therefore, the patient is further exposed to anastomotic leak or breakdown with even greater possibilities of abscess, fistula, peritonitis and death.

To obviate this contamination and its undesirable sequelae, numerous methods of closed or aseptic anastomoses were devised, many intricate, traumatic and physiologically unsound; others simple, relatively atraumatic and based upon sound knowledge derived from experimentation with various methods in animals.

The classification of Parker and Kerr[63] provides a useful summary of these methods:

1. Those in which an immediate opening is formed.
    a. Those in which the sutures are placed, most are tied, and the incision made at the last moment, followed by tying of the few remaining sutures.
    b. Those in which the incision is made at the beginning but kept closed by sutures, ligatures, clamps, etc. while the anastomosis is being formed.
2. Those in which a new stoma is formed by necrosis of tissue following anastomosis.

A more detailed account of the numerous methods and variations of closed anastomosis is beyond the scope of this review. Suffice it to say that great surgeons of our time, Holman,[64,65,66] Halsted,[67] Wangensteen,[68,69] Dennis,[20,21] Rankin,[70] Pringle,[71,72] Fraser[73,74] and innumerable others, have all been ardent advocates of this technique.

Regarding healing with the closed technique, Horine[75] observed that the inturn of intestine was absorbed between the third and fourth postoperative weeks. Scarff[76] noted disappearance of the devitalized flange at seven days, flattening of the flange with coverage of the mucosal defect at 14 days and difficulty in finding the site of anastomosis at 21 days. Fraser[74] found serous union of the peritoneum at 36 hours and complete healing by 76 days. In 1942, Gerbode,[77] studying gastrojejunal anastomoses in dogs, observed beginning epithelialization at 15 days, mucosal apposition at 14 to 17 days, and well formed mucosal glands by 21 days. The serosa healed well with a minimum of reaction

and Gerbode[77] concluded that closed anastomoses healed as well as open ones. Dennis[21] found more inflammation, greater inversion, slower mucosal regeneration, heavier scar and looser apposition of tissue following the open method. He therefore concluded that healing following closed anastomosis was at least as satisfactory as that following the open technique.

Irregardless of the lack of contamination, the studies cited above and clinical series reporting excellent results (Wangensteen,[68] Fraser[73]), with the advent of antibiotics many surgeons returned to the open anastomosis. Many feel that the more precise and delicate suturing, the more exact apposition, the strict hemostasis, the minimal trauma and small inturned flange secured by the open technique, lead to less inflammation, less anastomotic complications and more rapid and complete healing.

C. Single-layer versus multiple layer closure

Despite the fact that many earlier methods of anastomosis consisted of but one layer of sutures, the classic closure of this century has been the two or multiple tier technique. It was thought that multiple layers led to more inversion, greater strength and greater security of anastomosis. However, in 1923 Klose and Rosenbaum-Canné[78] demonstrated more tissue damage following the two-layer technique than was present in the one-layer technique. Martzloff and Suckow[30] found the most satisfactory healing in the anterior wall of gastrojejunostomies in dogs following closure with one layer of Halsted presection sutures. The classic papers of Gambee[79,80] in 1951 and 1956

introduced the single-layer, through and through inverting closure. Gambee felt that many sutures cause devascularization and necrosis of tissues and that, consequently, "a second layer of sutures only jeopardizes the blood supply of the tissue it inverts as well as creating a flange which may cause obstruction".[79] Buchin and Van Geertruyden[81] found more inflammation, necrosis and abscess formation in two-layer closures. Letwin and Williams[60] clearly demonstrated the superiority of the single layer closure. They observed more strangulation of tissue and more luminal stenosis in the two-layer variety. Histologically, the one-layer anastomosis showed more granulation tissue at five days and less inflammation, necrosis and abscess formation. Biochemically, the one-layer anastomosis had significantly higher hexosamine and hydroxyproline values at two, three and four days postoperatively.

These studies combined with the clinical reviews of Gambee,[80] Beling,[82] Bronwell et al.[83] and Olsen et al.,[18] attest the advantages of the one-layer technique. To quote Sako and Wangensteen,[84] "The use of multiple suture anastomosis is probably neither desirable nor necessary. As long as the inverted cuff does not evert upon mild pressure at the time of operation, additional sutures are not needed."

D. Inverted versus everted closure

Although this aspect of intestinal healing is the focus of much present day debate, the technique of eversion is far from new. Albucacis everted the intestinal mucosa in his ant head closure and Heister[85] described an everting technique in 1763. Henroz[86] everted the mucosa

with his metal ring stent and clamp, and Kummer[87] utilized a two-layer technique with separate closure of the mucosa and eversion of the remaining intestinal wall. Detailed study of the method, however, has occurred only recently. Hertzler and Tuttle[88] found prompt sealing and adequate healing in the esophagus and small bowel of dogs closed with a two-layer everting technique. They noted no more adhesions than with conventional techniques, no intraluminal sloughs or granulation, and no abscess formation. They felt that the everted union possessed greater strength and provided a more adequate union than the inverted technique. Healey et al.[89] found no differences in healing in inverted and everted closures. The everted closure was attended by more adhesions, the inverted closure by more luminal stenosis.

Ravitch and co-workers[90] studying staple closure of the stomach, duodenum and small bowel, noted that, contrary to accepted belief, healing did occur following mucosa-to-mucosa apposition, without excessive inflammation, obvious leakage, peritonitis or abscess formation. In a further study comparing five groups of dogs with inverting and everting closures, they noted more hemorrhage, edema, inflammation and necrosis in inverting closures. Mucosal covering was complete within 72 hours in everting closures, but delayed until two weeks in inverting anastomoses. Less pyogenic membrane and earlier cross-over of blood vessels were also noted in the everted groups. However, at three to six weeks, when the inverting anastomosis was well healed, zones of mucosal discontinuity and inflammatory reaction were found in the everted group. There was less luminal obstruction but greater adhesion formation in the everting anastomoses. After still further studies with the everting

technique, they concluded that the bowel will heal primarily with mucosa-to-mucosa apposition, and does not rely on adhesions for adequate union. Throughout their studies they were most impressed with the technical ease and large lumen of the everted technique.

Getzen, Roe and Holloway[91,92,93] demonstrated less stasis and edema in everting anastomoses in dogs. Both everting and inverting groups were sealed by fibrin within 24 hours, both showed mucosal regeneration in seven to 21 days and no difference was detected in collagen formation. They found the tensile strength of the everting anastomosis to be significantly greater up to 21 days and attributed this difference to the presence of greater edema in the inverted variety. They believed the everting anastomosis to have a better blood supply due to less need to strip intestinal fat to perform the anastomosis accurately, less blood vessel angulation at the stoma and no turning in of the mesentery at the anastomosis. They concluded, however, that there was no significant difference in the healing of everting or inverting closures.

Mellish[94] noted no significant difference in the healing of inverting and everting groups, other than the presence of more adhesions around everting closures. He was unable to demonstrate any significant degree of stenosis in the inverting closure.

Contrary to the favorable studies of Ravitch et al.,[90] Getzen et al.[91] and others, are those of Martzloff and Suckow,[30] Hamilton,[95] Loeb,[96] Trueblood et al.[26] and Gill et al.[97] Martzloff and Suckow found appositional inclusions in techniques with mucosal eversion. Hamilton concluded that the Gambee anastomosis was superior to the

everted technique in dogs. Loeb found the everted anastomosis to be the weakest variety of those he tested, and also noted more adhesions and microabscesses associated with the everted group. Trueblood et al. observed denser adhesions, slower mucosal healing and diminished bursting strength in everted anastomoses when compared with inverted closures. Gill et al. found more microabscesses and inflammatory reaction in their everted group and concluded that the "immediate postoperative sealing of the everting anastomosis was less than adequate".

The available data on everting anastomosis, then, remains conflicting.

In conclusion, it may be stated that the manner in which a technique is performed may often be more important than the technique itself. Gentle handling of tissues, adequate hemostasis, prevention of contamination, proper placement and tying of sutures, avoidance of tension and preservation of blood supply are all cardinal factors in achieving optimal intestinal healing.

However, the greatest requirement remains the investigation of the basic principles of intestinal healing. When these parameters are more thoroughly understood, perhaps the methods of achieving these ideals will be more easily and directly attained.

OBJECTIVES

Adhesions at the site of intestinal anastomosis may serve one, two, or all of three possible functions:

1. They may serve as vascular grafts to ischemic areas of intestine.
2. They may serve to isolate areas of intestinal leakage from the general peritoneal cavity.
3. They may serve as a simple mechanical support to the anastomosis in the initial stages of the healing process.

The purposes of this study are essentially twofold:

1. To investigate the mechanical support offered to the anastomosis by the surrounding adhesions.
2. To compare the contribution of adhesions to the overall strength of anastomoses constructed by both the inverting and everting techniques.

Incidentally, this study offers other parameters by which inverted and everted anastomoses may be compared.

METHOD

Adult male Sprague-Dawley rats were used throughout both experiments. Rats were chosen because they are hardy, reasonably resistant to peritonitis, and have an intestinal microflora similar to that of man. They are also readily available, of low cost, and represent a relatively homogeneous group. Sprague-Dawley rats were used in particular so as to allow a close comparison with data previously collected in this laboratory. The mean weight of rats in Experiment #1 was 280.5 grams on arrival at the laboratory. In Experiment #2, the mean weight of animals upon arrival was 289.5 grams. All rats were fed a standard Purina laboratory diet (approximately 15 grams per rat per day) with water ad libitum. The animals were caged individually and were allowed a minimum of eight days in which to settle in their cages prior to surgery.

A. EXPERIMENT #1

Eighty animals were randomly allocated into ten groups of eight rats each, and each group of eight was further subdivided into two groups of four. All animals underwent a standard operation, one group (8) being operated upon each day. All operations were completed within a twelve day interval. The animals were fasted for 24 hours preoperatively. Immediately prior to surgery the animals were weighed, anaesthetized with intraperitoneal sodium pentobarbital[*] in a dosage of 39 mgm./kg. and depilated with electric clippers. The abdomen was prepared with 10% povidone-iodine.[¶]

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[*] Diabutal - Diamond Laboratories Inc., Des Moines, Iowa.

[¶] Betadine - The Purdue Frederick Co. Ltd., Toronto, Ontario.

At operation, the peritoneal cavity was opened through a two centimetre midline incision beginning at mid-abdomen and extending to within two centimetres of the symphysis pubis. Upon entering the peritoneal cavity the caecum was identified as a landmark and a segment of ileum 15 centimetres proximal to the ileo-caecal valve isolated on the anterior abdominal wall. The marginal artery and vein immediately subjacent to this isolated segment were then ligated in continuity with 6-0 black silk. The mesentry was opened to the first vascular junction and a segment of ileum one to two centimetres in length excised. An open technique was followed throughout the procedure. Great care was taken to have a major branch of the superior mesenteric artery in close proximity to both the proximal and distal ends of bowel to be anastomosed. Care was also taken to resect sufficient bowel that both ends to be anastomosed bled freely following resection. Lembert[5] stay-sutures of 6-0 black silk were then inserted at the mesenteric and antimesenteric borders of the bowel. Four interrupted 6-0 silk Lembert sutures were inserted between the stay-sutures anteriorly, the bowel turned over, and four similar sutures placed in the posterior wall of the anastomosis (Fig. 1). The inverted cuff achieved by this method was approximately one millimetre in width. Following completion of the anastomosis, the suture line was inspected and an additional stitch inserted if deemed necessary. Patency of the anastomosis was confirmed by invagination of a closed forcep through the stoma and the bowel returned to the right lower quadrant of the abdomen. The defect in the mesentery was not sutured. The musculo-fascio-peritoneal layers of the anterior abdominal wall were closed in one layer with three interrupted

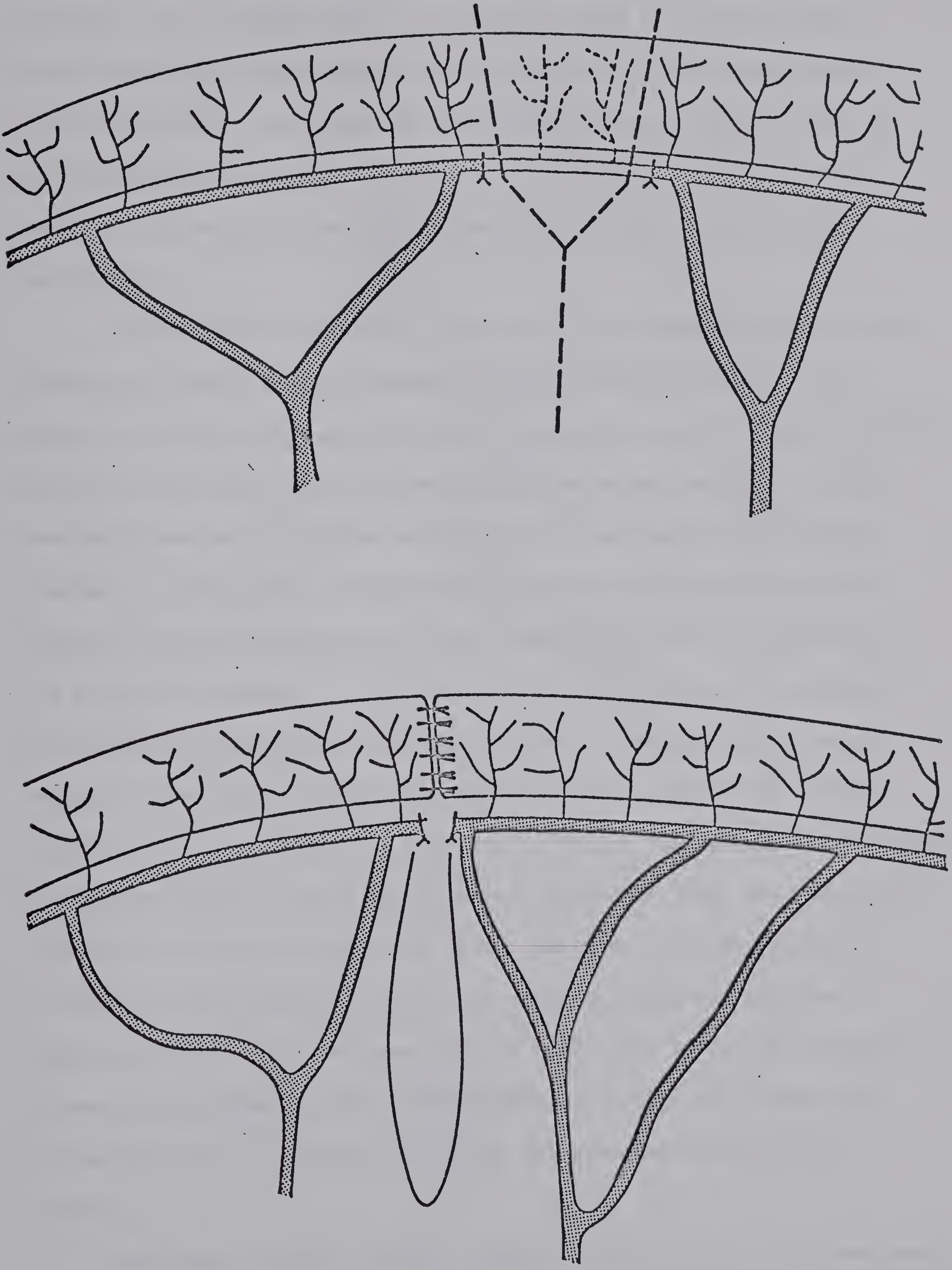

Fig. 1 General technique of intestinal anastomosis.

sutures of 3-0 chromic catgut and the skin with five interrupted sutures of 3-0 chromic catgut. The animals were allowed food and water immediately after operation and inspected several times daily until sacrificed. One group of animals (8) was sacrificed at each of the following postoperative intervals: six hours, 12 hours, 24 hours, two days, three days, four days, five days, six days, eight days, and 10 days.

At the time of sacrifice, the animals were again weighed and the abdomen was widely opened through a parabola-shaped incision. The degree of obstruction proximal to the anastomosis and the extent to which adhesions surrounded the anastomosis were noted and recorded. A five centimetre segement of ileum centred on the anastomosis was excised. However, in each group of animals (8), one half (4) had the adhesions removed from the anastomosis by sharp dissection prior to excision of the anastomotic segment. In the remaining four animals, the adhesions surrounding the anastomosis were left intact. Immediately following removal of the ileal segment, its distal end was occluded by a silk ligature and the proximal end attached to tubing leading via a Y-connector to a Harvard Infusion pump and a mercury manometer (Fig. 2). Water was infused at a constant rate of 61.20 cc. per minute and the pressure at which the anastomosis ruptured and water extruded was recorded. Infusion at this rapid rate was used to offset the effect of prolonged distension described by Sako and Wangensteen;[84] i.e. the longer the distending force is applied, the lower the pressure required for bursting.

Following pressure testing a specimen consisting of the anastomosis

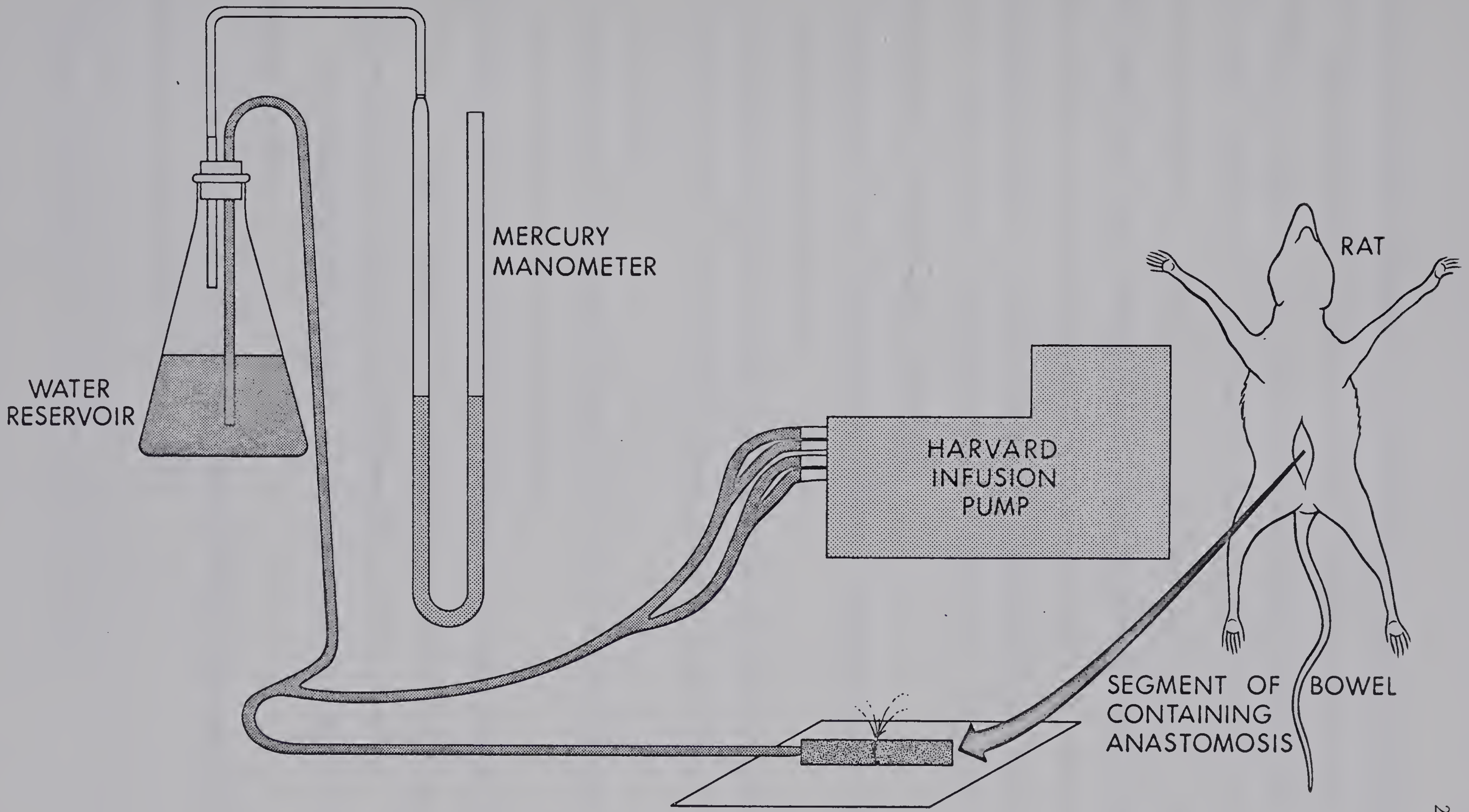

Fig. 2 Apparatus for bursting pressure determination

together with one centimetre of bowel above and below the anastomosis was submitted for hydroxyproline analysis. These specimens were immediately weighed, quick frozen, and left frozen for ten days. At ten days, the specimens were removed from the freezer, homogenized and mixed with 10 ml. of 6N HCl and autoclaved for three hours at 124°C. The samples were then neutralized (to pH 7.0---phenolphthalein indicator) with 3N NaOH, activated carbon added, and the suspension passed through a micropore filter. A 0.1 ml. aliquot of the filtrate was diluted to 2.0 ml. with 1.9 ml. of distilled water. The 2.0 ml. aliquot was then subjected to the following procedures:

1. Addition of 1.0 ml. of $CuSO_4$ and 1.0 ml. of NaOH (reagents mixed immediately prior to use).
2. Addition of 1.0 ml. of 6% H_2O_2 and agitation for five minutes.
3. Addition of 0.1 ml. of 0.05 M ferrous sulfate and agitation for six minutes.
4. Addition of 4.0 ml. 4N H_2SO_4 and 2.0 ml. 4% p-dimethyl-amino-benzaldehyde and mixture by swirling.

The end solution was subsequently incubated in a water bath at 70°C for 16 minutes. After cooling, the solution was measured against a blank solution (water) at 560 mμ. in a Beckman DU spectrophotometer.* [98,99]

The hydroxyproline content was determined by reference to a standard curve.

All data from this experiment were analyzed for statistical significance using the Students' t test.

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* Beckman Instruments Inc., Schiller Park, Illinois.

Any animals dying in the course of the experiment, or any in which the bowel wall was inadvertently damaged during dissection of adhesions were replaced (to the limit of reserve animals).

B. EXPERIMENT #2

Once again, eighty animals were randomly allocated into ten groups of eight animals and each group was further subdivided into two groups of four rats. One group of animals (8) was operated upon each day and all operations were completed in a ten day interval.

Preoperatively, the animals were prepared in an identical manner to that of Experiment #1. The operative technique was also identical to that of Experiment #1, with the exception of the technique of anastomotic construction. In these rats, the anastomosis was constructed in an everting manner as described by Getzen, Roe and Holloway.[91] Simple sutures of 6-0 black silk were initially placed at the mesenteric and antimesenteric borders of the intestine. Four simple sutures of silk were then placed both anteriorly and posteriorly between the stay-sutures. The mucosa of the bowel was allowed to evert for the entire circumference of the anastomosis. An additional suture was inserted if necessary, the patency of the stoma confirmed, and the bowel returned to the right lower quadrant of the abdomen.

The postoperative routine was also identical to that of Experiment #1 and one group of animals (8) was sacrificed at identical intervals of six hours, 12 hours, 24 hours, two days, three days, four days, five days, six days, eight days, and 10 days. The extent of adhesion formation and obstruction proximal to the anastomosis were noted. Again, at the time of sacrifice, one half the animals (4) had the adhesions

surrounding the anastomosis removed by sharp dissection while the remaining one half (4) had the adhesions surrounding the anastomosis left intact. A five centimetre segment of ileum centred on the anastomosis was then removed and its bursting pressure measured as in Experiment #1. All anastomoses were then submitted for routine histological preparation. Sections of all anastomoses stained with hematoxylin and eosin were examined. Animals dying during the experiment, or in which the anastomosis was damaged during removal of adhesions, were replaced. All data were analyzed for statistical significance.

RESULTS

A. EXPERIMENT #1 (INVERTED ANASTOMOSES)

The healing curves of both groups of anastomoses (anastomosis intact and anastomosis with adhesions removed by dissection) followed a similar pattern (Fig. 3). From six hours until 12 hours postoperatively, the bursting pressures of the anastomoses rose rapidly. After 12 hours, the bursting pressures declined, reaching a low peak at three days. The strength of the anastomoses then increased rapidly from three days to six days, followed by a more gradual rise from six to 10 days. At six hours and 12 hours the mean bursting pressures of those anastomoses in which adhesions had been removed by dissection were greater than that of those in which the anastomoses were left intact. These differences were not statistically significant. After 12 hours, however, the intact anastomoses were stronger than those in which the adhesions had been removed. This difference persisted until the experiment was terminated at 10 days postoperatively. As may be noted in Table I, these results are statistically significant in the time interval from 24 hours to five days. Thereafter, the difference in bursting pressures was not significant statistically.

If the percentage contributions of adhesions to the mean bursting pressures of the anastomoses are calculated using the formula

$$\frac{\text{Mean strength of intact anastomoses - mean strength of anastomoses with adhesions removed}}{\text{Mean strength of intact anastomoses}} \times 100$$

and illustrated graphically (Fig. 4), it is again apparent that the maximal contribution of adhesions to withstanding pressure distension

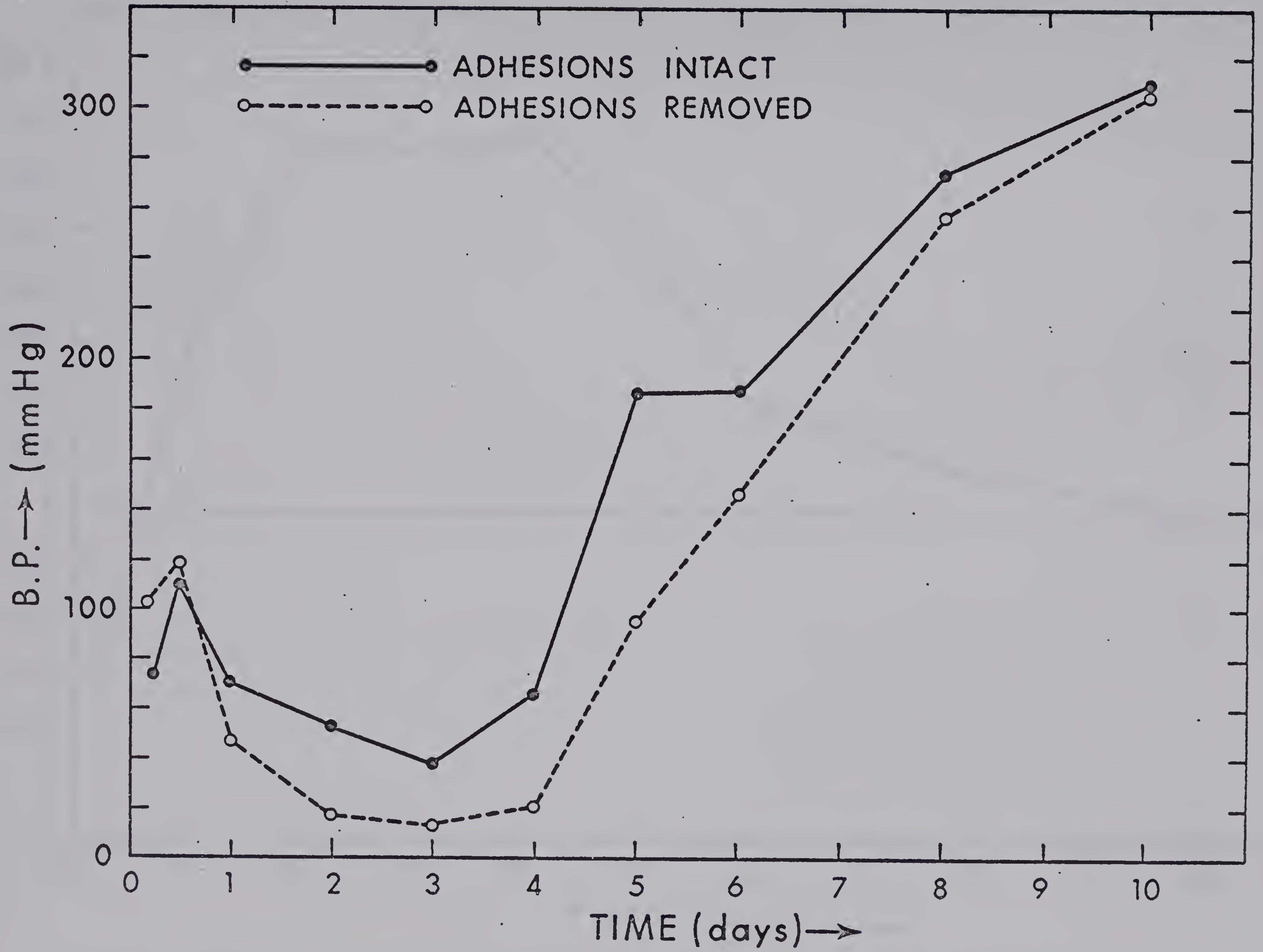

Fig. 3 Mean bursting pressures of inverted anastomoses.

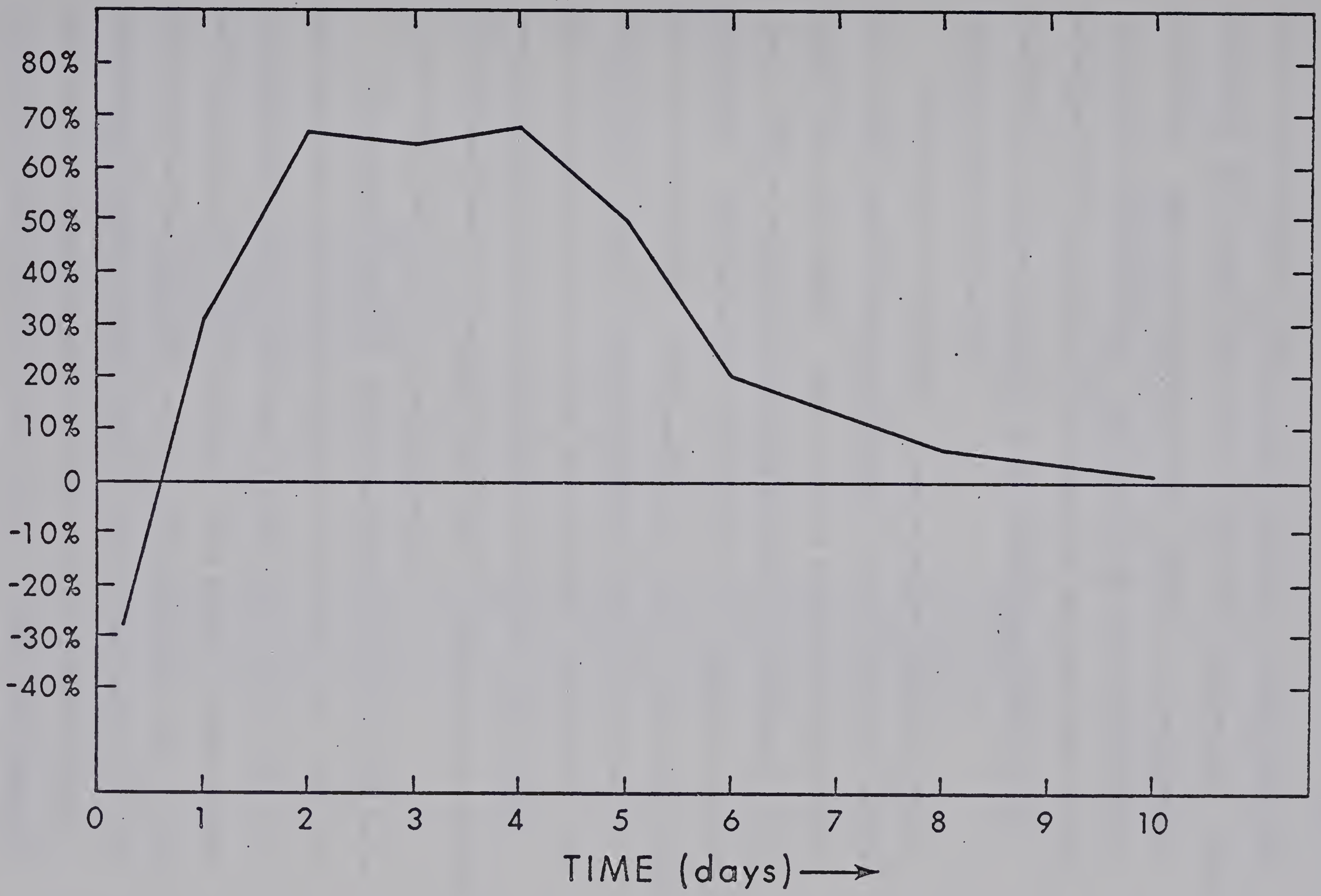

Fig. 4 Percentage contribution of adhesions to the total strength of inverted anastomoses.

occurs from 24 hours to five days postoperatively, at which time they contribute 32% to 68% of the total strength of the anastomosis. Prior to 24 hours, adhesions apparently do not contribute to the bursting strength of the anastomoses. From five to 10 days postoperatively, adhesions still contribute to the strength of the anastomosis but this contribution declines gradually and is far less marked than in the 24 hour to five day interval.

At the time of sacrifice, it was noted that adhesions form in great number around inverted anastomoses at all stages of the healing process that were studied. Sixty of the 78 animals included in this study (77%) had adhesions surrounding the entire circumference of the anastomosis. Eighteen animals (23%) did not have adhesions surrounding the entire circumference of the anastomosis (Fig. 5). This latter group varied from one animal in which no adhesions were present to one in which the adhesions covered 7/8 of the anastomotic circumference, the remaining animals falling between these two extremes. Most animals with the anastomosis incompletely surrounded by adhesions were sacrificed in the first four days of the healing process.

In the total group of inverted anastomoses (78), 37 (47%) had a bursting pressure greater than the mean of their group, two (3%) had a bursting pressure equal to the mean of their group, and 39 (50%) had a bursting pressure less than the mean of their group. In those animals in which adhesions completely surrounded the anastomosis (60), 26 (43%) had bursting pressures greater than the mean of their group, one (2%) had a bursting pressure equal to the mean, and 33 (55%) had bursting pressures less than the mean of their group. Of those with adhesions

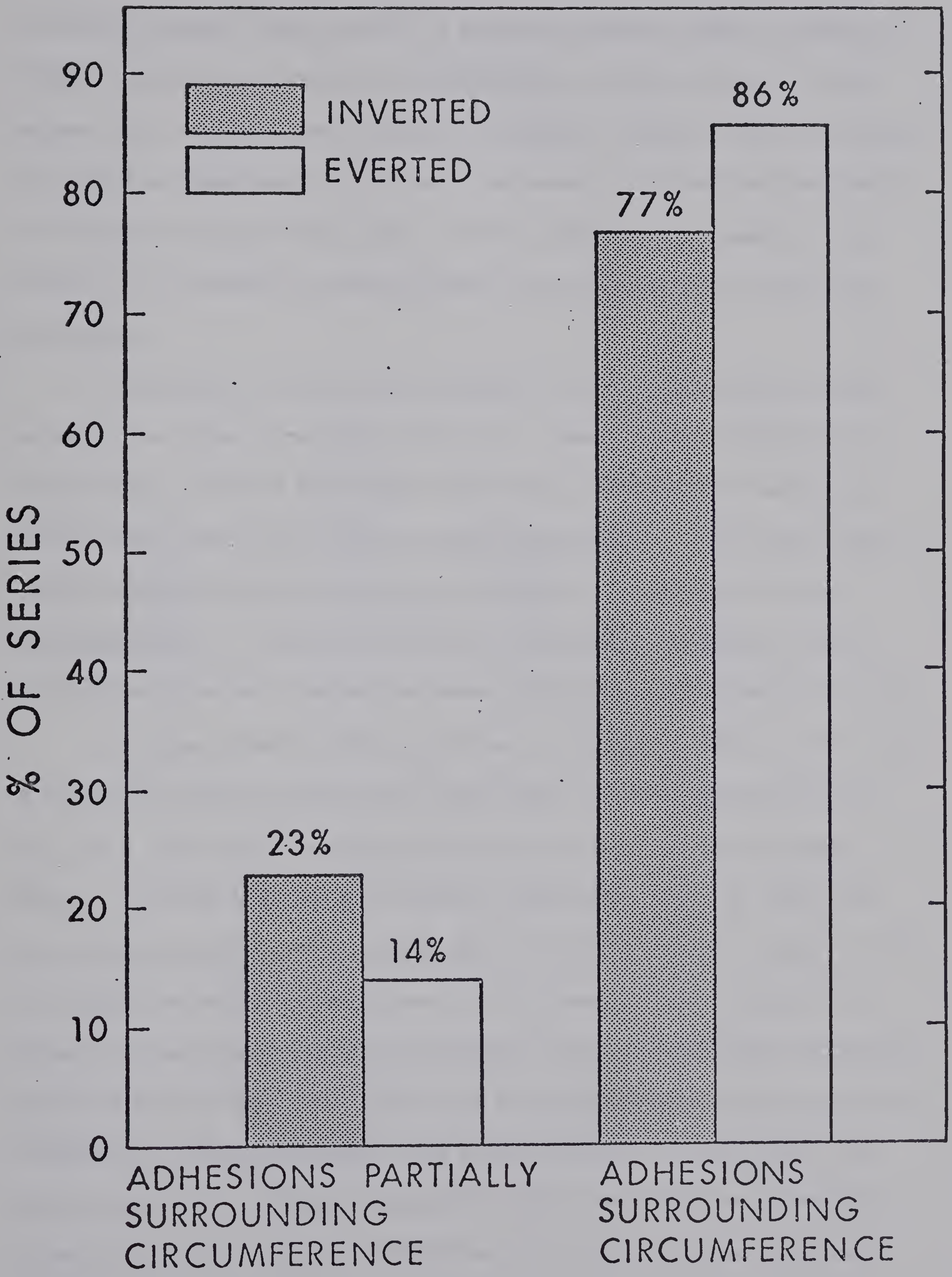

Fig. 5 Incidence of adhesions following inverted and everted anastomoses.

incompletely surrounding the anastomosis (18), 11 (61%) had bursting pressures greater than, one (6%) a bursting pressure equal to, and six (33%) a bursting pressure less than the mean of their group. It would appear then, that the mere absence of adhesion formation does not weaken the inverted anastomosis. In fact, the absence of adhesions may denote an integrally strong bowel wound. This is not to say, however, that removal of an adhesion already formed does not weaken the underlying anastomosis.

The degree of obstruction proximal to the anastomosis was also noted at the time of sacrifice (Fig. 6). Twenty animals (26%) had no obstruction, 32 (41%) had slight obstruction, 18 (23%) had moderate obstruction, and eight (10%) had marked obstruction. All animals with marked proximal obstruction were sacrificed at or before 24 hours postoperatively. Inverted anastomoses, therefore, frequently lead to significant proximal obstruction when performed in the ileum of the rat.

In those animals with no proximal obstruction (20), 11 (55%) had a bursting pressure greater than, none had a bursting pressure equal to, and 9 (45%) had a bursting pressure less than the mean of their group. In those with slight proximal obstruction (32), 16 (50%) had a bursting pressure greater than, none a bursting pressure equal to, and 16 (50%) a bursting pressure less than the mean of their group. In those with moderate proximal obstruction (18), six (33%) had a bursting pressure greater than, one (6%) had a bursting pressure equal to, and 11 (61%) had a bursting pressure less than the mean of their group. In those with marked proximal obstruction (8), four (50%) had a bursting pressure greater than, one (12.5%) had a bursting pressure equal to,

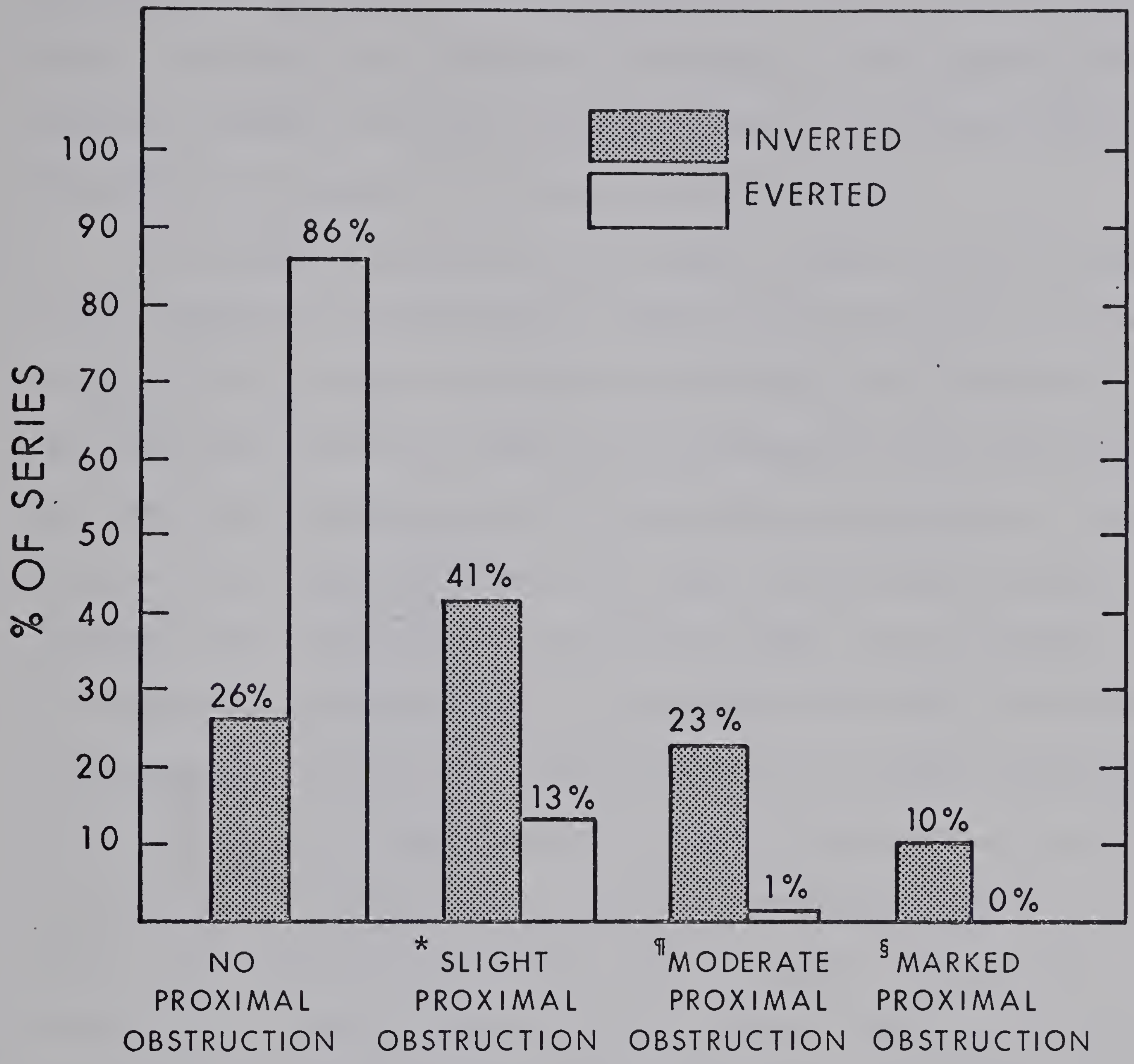

Fig. 6 Incidence of proximal bowel obstruction following inverted and everted anastomoses.

[*] Slight proximal obstruction - dilatation of the bowel for a short distance above the anastomosis.

[¶] Moderate proximal obstruction - dilatation of the entire small bowel above the anastomosis.

[§] Marked proximal obstruction - massive dilatation of the stomach and entire small bowel above the anastomosis.

and three (37.5%) had a bursting pressure less than the mean of their group. Therefore, with the possible exception of those animals with moderate proximal obstruction, varying degrees of obstruction did not significantly accelerate or retard the healing process.

The effect of adhesions on the degree of obstruction was assessed in two fashions. As illustrated in Table II, the percentages of animals, with the varying degrees of obstruction mentioned, were calculated for the two groups; those with adhesions surrounding the entire anastomosis and those with adhesions partially surrounding the anastomosis. These figures do not differ appreciably from those for the entire group of animals in this experiment. In the second method, the percentages of animals with adhesions totally or partially surrounding the anastomosis were calculated for the four groups, those with no proximal obstruction, those with slight proximal obstruction, those with moderate proximal obstruction, and those with marked proximal obstruction (Table III). Again, these figures do not differ appreciably from those for the total group of animals with inverted anastomoses. Adhesions then, do not appear to play a prominent role in postoperative intestinal obstruction at this stage of the healing process (the first 10 days).

Of the ninety rats operated upon, 12 (13%) died within the 10 day study period (Fig. 7). All 12 rats dying had massive intestinal obstruction proximal to the anastomosis. In two cases, there was also leakage from the anastomosis and generalized peritonitis.

As indicated in Table IV, there was no significant weight differences between the two groups of animals studied. Although every animal did not gain weight between operation and sacrifice, the mean weight of animals in both groups increased from arrival to operation and from operation to

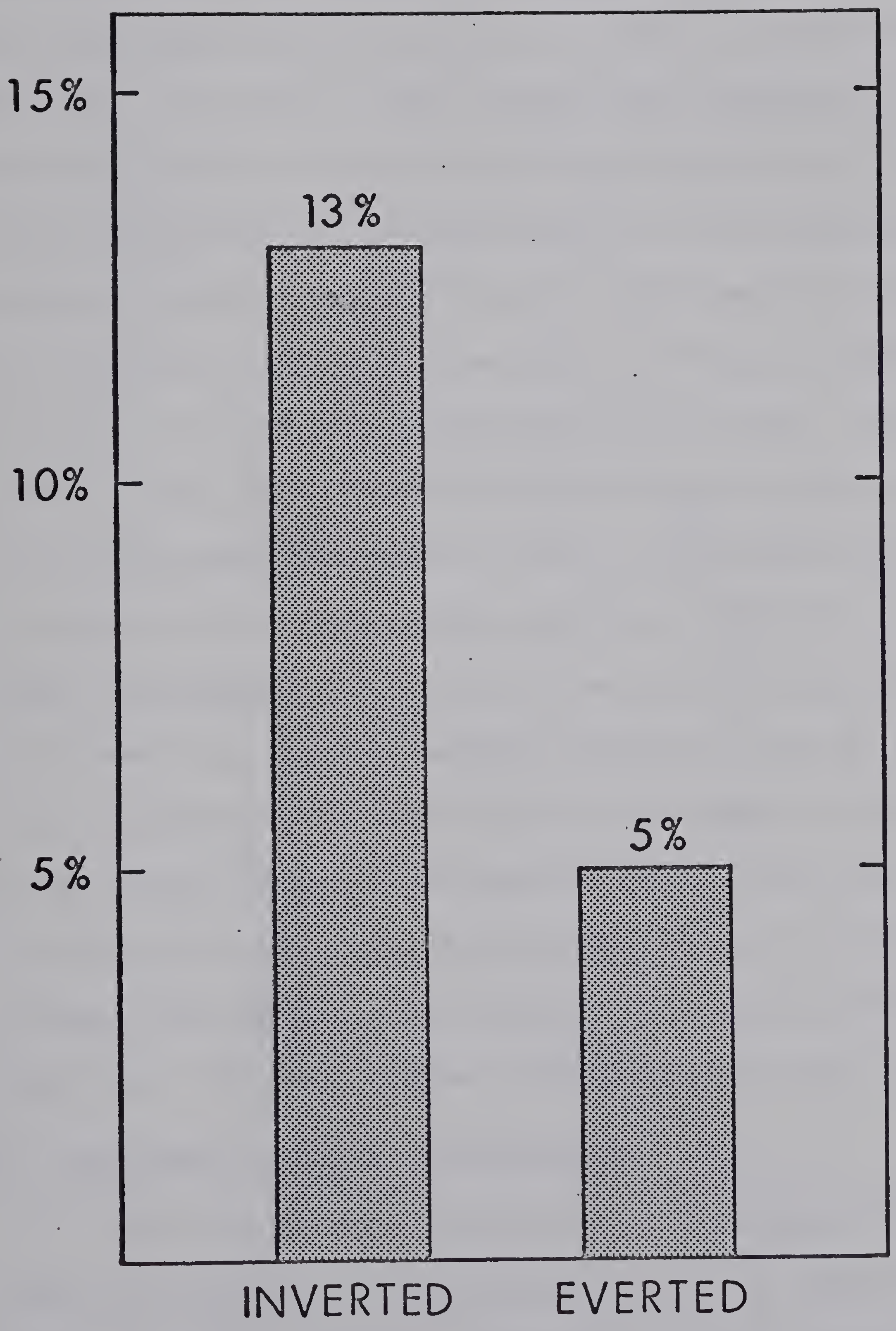

Fig. 7 Mortality rate following inverted and everted anastomoses.

sacrifice.

Fig. 8 illustrates the mean hydroxyproline concentrations of inverted anastomoses. The hydroxyproline concentration of the intact anastomoses rose from six to 24 hours and then fell, reaching a minimum concentration at three days postoperatively. From three to five days the concentration rose slowly, followed by a more rapid increase from five to six days. After six days the concentration fell off somewhat at eight days, after which it rose slightly until 10 days. The curve of hydroxyproline concentrations for those anastomoses in which adhesions had been removed followed a similar pattern with the exceptions of a falling concentration between six and 12 hours and a more marked increase in concentration between five and six days. With the exception of the six day values, the differences in hydroxyproline concentrations in the two groups (anastomosis intact and anastomosis with adhesions removed) were not statistically significant (Table V). The markedly higher concentration at six days in the group with adhesions removed is attributed to an error in sampling technique. With the care taken to assure integrity of the anastomosis during removal of adhesions, a part of the fibrous portion of the adhesion may have been left in contact with the bowel wall. This would have the effect of increasing total collagen (and hydroxyproline) while at the same time decreasing the total mass. The concentration of hydroxyproline would therefore increase.

B. EXPERIMENT #2 (EVERTED ANASTOMOSES)

The healing curves of both groups of anastomoses (anastmosis intact and anastomosis with adhesions removed by dissection) not only followed a pattern similar to each other but also closely simulated

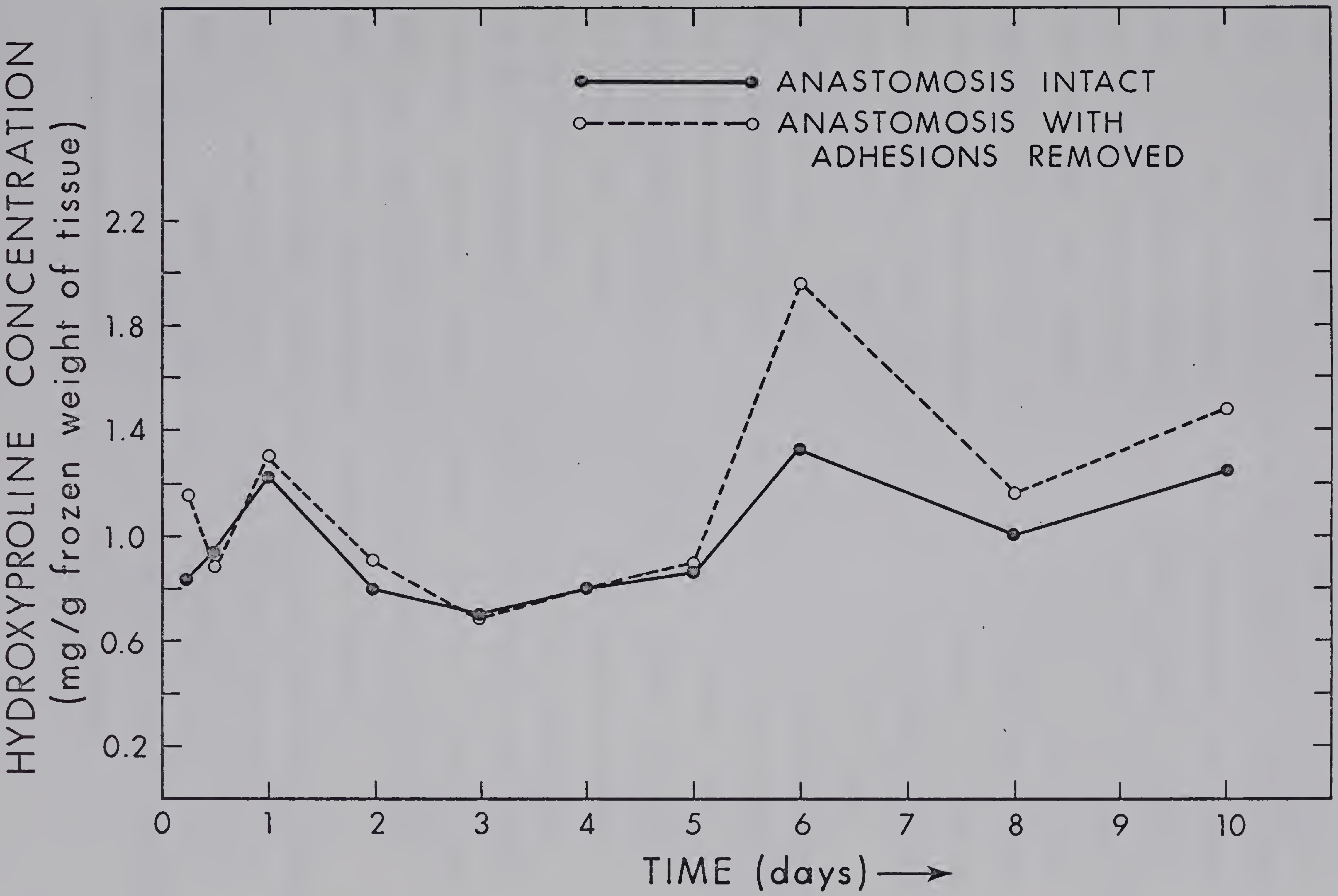

Fig. 8. Mean hydroxyproline concentrations of inverted anastomoses.

the healing curves found in the two groups with inverted anastomoses (Fig. 9). Both groups of anastomoses again increased in strength from six to 12 hours postoperatively. After 12 hours, however, the anastomotic strength began a sharp decline, reaching a minimum at two days. In the intact anastomoses, the strength of the wound increased gradually from two to four days, rapidly from four to six days, and more slowly again from six to 10 days. In the anastomoses with adhesions removed, the strength of the wound remained relatively low from two to five days, rose very rapidly between five and six days, and then tapered to a more gradual rate of increase from six to 10 days. The mean bursting pressures of those anastomoses from which adhesions had been dissected were again greater than the mean bursting pressures of those anastomoses left intact at the six and 12 hour postoperative intervals. These differences were not statistically significant. However, the intact anastomoses were stronger than those from which adhesions had been removed from 24 hours onward until termination of the experiment at 10 days. This difference was statistically significant in the period from one to five days following operation. Although the intact anastomoses were also stronger from six to 10 days postoperatively, these differences were not statistically significant (Table VI).

The percentage contributions of adhesions to the overall strength of the anastomoses were again calculated using the same formula as in Experiment #1, and the results expressed graphically (Fig. 10). It is again apparent that from 24 hours to five days postoperatively, adhesions contribute significantly (45% to 79%) to the total strength of the

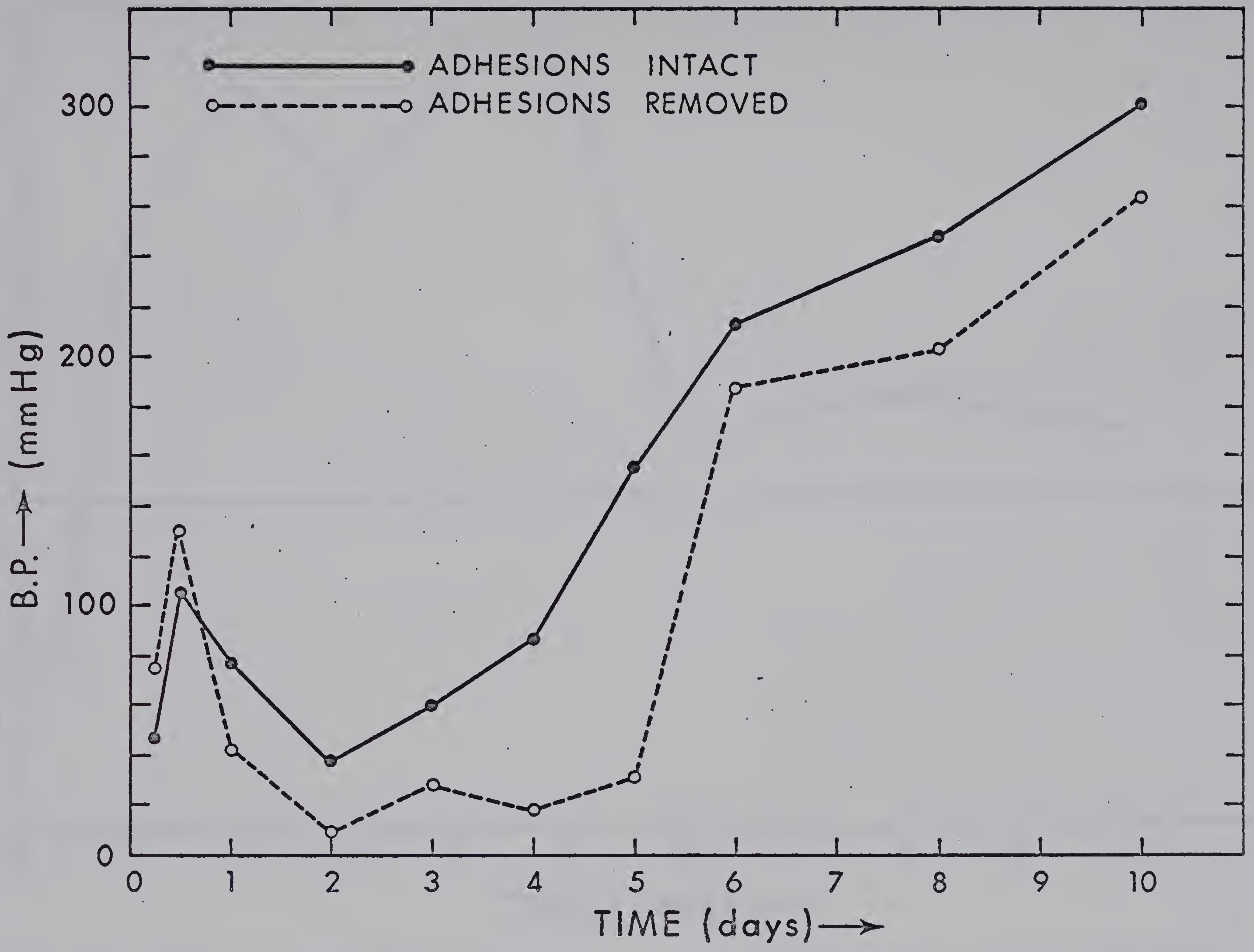

Fig. 9 Mean bursting pressures of everted anastomoses.

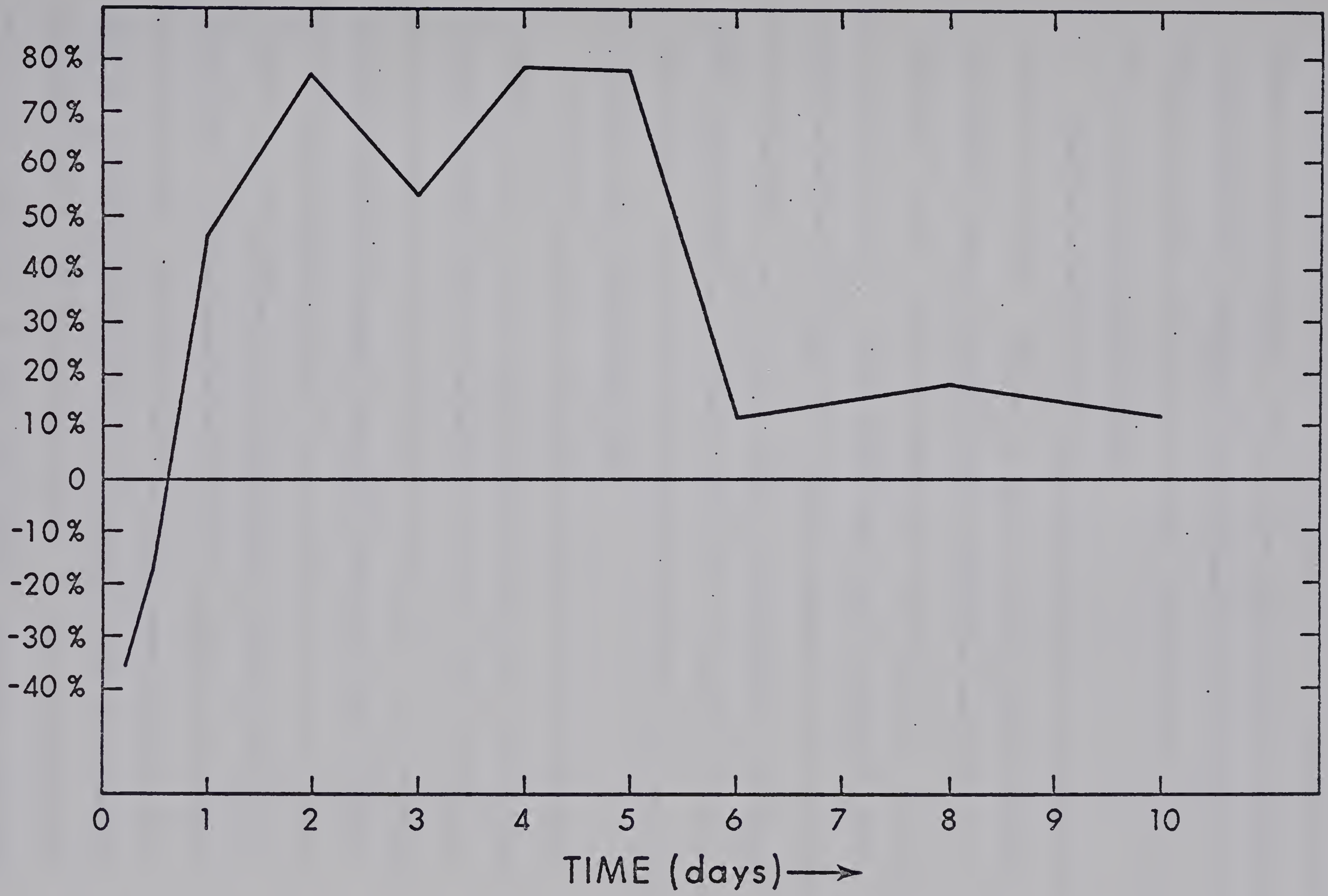

Fig. 10 Percentage contribution of adhesions to the total strength of everted anastomoses.

anastomosis. Prior to 24 hours the adhesions did not contribute to the strength of the anastomosis. Between five and six days, the contribution of adhesions to the strength of the anastomosis fell off rapidly, then remained at a plateau from six to 10 days, contributing only fractionally to the overall anastomotic strength.

Numerous adhesions were found around the everted anastomoses at the time of sacrifice. Sixty-eight (86%) of the 79 animals included in this study had adhesions completely surrounding the anastomosis. In the remaining 11 animals (14%), the anastomosis was incompletely surrounded by adhesions (Fig. 5). In one animal there were no adhesions and in two the adhesions surrounded 7/8 of the circumference of the anastomosis. In the remainder, the adhesions covered a circumference of the anastomosis between these two extremes. Once again, the majority of animals with adhesions incompletely surrounding the anastomosis were sacrificed in the first four postoperative days.

In the total group of everted anastomoses (79), 39 (49%) had a bursting pressure greater than the mean of their group, one (1%) had a bursting pressure equal to the mean of its group, and 39 (49%) had a bursting pressure less than the mean of their group. In those animals in which adhesions surrounded the entire anastomosis (68), 36 (53%) had a bursting pressure greater than, one (1%) had a bursting pressure equal to, and 31 (46%) had a bursting pressure less than the mean of their group. In those anastomoses that were incompletely surrounded by adhesions (11), three (27%) had a bursting pressure greater than, none had a bursting pressure equal to, and eight (73%) had a bursting pressure less than the mean of their group. In the total group with everted anastomoses and in those with adhesions completely surrounding

the anastomosis, this data does not differ significantly, nor does it differ significantly from comparable data in Experiment #1. However, the figures from those anastomoses incompletely surrounded by adhesions, differ greatly from those in the total group with everted anastomoses and from those in Experiment #1. The available material suggests that lack of adhesion formation around an everted anastomosis may weaken the anastomosis. This is contradictory to the findings with inverted anastomoses. However, the small number of animals in these groups defies the formation of valid conclusions.

In the total group of animals with everted anastomoses, obstruction proximal to the anastomosis was found less frequently and to a lesser degree than in the total group with inverted anastomoses. Sixty-eight (86%) had no obstruction proximal to the anastomosis, 10 (13%) had slight proximal obstruction, and one (1%) had moderate proximal obstruction (Fig. 6). No animals had marked obstruction proximal to the anastomosis. The one animal with moderate proximal obstruction was sacrificed 24 hours following surgery.

In the animals with no proximal obstruction (68), 34 (50%) had a bursting pressure greater than the mean of their group, one (1%) had a bursting pressure equal to the mean of its group, and 33 (49%) had bursting pressures less than the mean of their group. In those with slight proximal obstruction (10), five (50%) had a bursting pressure greater than, and five (50%) had a bursting pressure less than the mean of their group. The one animal with moderate proximal obstruction had a bursting pressure less than the mean of its group. As in the animals with inverted anastomoses, it would appear that the

presence of slight proximal obstruction is not detrimental to the healing process. However, because only one animal had moderate proximal obstruction, no conclusion regarding the effect of this degree of obstruction on the healing of everted anastomoses has been drawn.

The effect of adhesions on the degree of obstruction was again assessed in two fashions. As illustrated in Table VII, the percentages of animals with the varying degrees of obstruction, were calculated for the two groups, those with adhesions surrounding the entire anastomosis and those with adhesions only partially surrounding the anastomosis. It is evident from this data that the number of adhesions surrounding the anastomosis does not play a role in the degree of obstruction observed. In the second method of assessment (Table VIII), the percentages of animals with adhesions totally or partially surrounding the anastomosis were calculated for the three groups, those with no proximal obstruction, those with slight obstruction, and those with moderate obstruction. Once again, no conclusions were drawn from the group with moderate proximal obstruction because it contained but one animal. If the percentages for those with no or slight proximal obstruction are compared to those for the total group with everted anastomoses (Table VIII), one may conclude further that the number of adhesions surrounding the anastomosis is not a determining factor in the degree of obstruction observed. These conclusions are in agreement with those drawn from Experiment #1. However, it should be noted that one animal died as a result of torsion of the small bowel around an adhesion. Adhesions then, even very early in the healing process, are not totally innocuous.

Four of the 83 rats operated upon (5%) died within the 10 day study period (Fig. 7). As just mentioned, one animal died of intestinal obstruction following torsion around an adhesion. Of the remaining three deaths, two animals died of anastomotic leakage and generalized peritonitis, and in one the cause of death was not apparent.

No significant weight differences in the two groups of animals were noted (Table IV). The mean weights of animals in both groups increased from arrival to operation and from operation to sacrifice. However, not all animals had a progressive gain in weight throughout the course of the experiment.

Histological sections of all anastomoses in Experiment #2 revealed no difference in the two groups (anastomosis intact and anastomosis with adhesions removed) apart from the presence or absence of overlying adhesions. Initially the anastomoses showed signs of acute inflammation with engorgement of vessels and infiltration of polymorphonuclear leukocytes. Tissue necrosis and edema were also prevalent in the early time period following surgery. About the third postoperative day, however, the edema and inflammation began to subside although they persisted to some degree throughout the 10 day interval. Also by the third day, lymphocytes and macrophages were the prevalent cells in the wound. Epithelial outgrowth over the ulcerated mucosa was first noted in the four day specimens and in only a few of the eight and 10 day specimens was this covering complete. This outgrowth was initially squamous and later cuboidal and on occasion was seen to undermine the granulation tissue present. At no time in the 10 days were columnar cells, goblet cells, villi or intestinal glands noted in the regenerating

epithelium. Collagen fibres were recognized at five days postoperatively and increased progressively in number until termination of the experiment. Interestingly, a reasonable proportion of the collagen seen in the intact anastomoses, appeared to form in the adhesions surrounding the anastomosis. Removal of the adhesion then, might be expected to lessen the overall collagen content of the healing anastomosis. Microabscesses were rare and no microfistulae were seen. An occasional inclusion cyst was noted forming in the vicinity of a strand of silk. The everted epithelium gradually necrosed and was not a prominent feature in the eight and 10 day specimens, most of this epithelium having already sloughed. No cysts were noted in association with the everted mucosa.

C. COMPARISON OF DATA

A statistical comparison of bursting pressures between animals in Experiment #1 and Experiment #2 was carried out, those with anastomoses intact in Experiment #1 being compared to those with anastomoses intact in Experiment #2, and those with adhesions removed in Experiment #1 being compared with the similar group in Experiment #2. This data is tabulated in Table IX. In the animals with intact anastomoses, the inverted were stronger at some time intervals while the everted were stronger at other time intervals. However, only at three days was the difference in mean bursting pressures statistically significant. In this case the everted anastomoses were the stronger. This may be attributable to a longer persistence of inflammation and edema in the inverted anastomoses. Alternatively, there may in fact be no real difference in the strengths of inverted or everted anastomoses and this isolated result

may fall outside the limits of probability mentioned. At three days the everted anastomoses from which the adhesions had been removed were also stronger than the comparable inverted anastomoses but this difference was not statistically significant.

In those anastomoses in which the adhesions had been removed by dissection, the inverted anastomoses were again stronger at some time intervals while the everted were stronger at other time intervals. At five days postoperatively, the inverted anastomoses were significantly stronger than the everted anastomosis. The intact inverted anastomoses were also stronger than intact everted anastomoses at five days postoperatively but this difference was not statistically significant. Differences in anastomoses with adhesions removed were not statistically significant at intervals other than five days.

Of the ten time intervals studied, seven (70%) had a positive correlation as to whether the inverted or everted anastomosis was stronger in both groups (anastomosis intact and anastomosis with adhesions removed). In the remaining three intervals (30%), the intact anastomosis was stronger in the everted group while the anastomosis with adhesions dissected was stronger in the inverted group, or vice versa.

D. INCIDENTAL OBSERVATIONS

Three incidental observations common to both Experiment #1 and to Experiment #2 will be briefly mentioned.

1. At eight and 10 days the bowel did not invariably rupture at the site of anastomosis. At eight days the rupture occurred either at the site of anastomosis or immediately adjacent to it. At 10 days, the rupture occurred at the anastomosis, adjacent to the anastomosis, or at

some distance from the anastomosis in normal bowel wall.

2. During testing of the anastomosis by pressure distension, several isolated cases were noted in which the adhesions began to strip off the anastomosis as the bowel inflated. This was usually seen in the early postoperative period and often began at relatively low pressures (50-100 mm. Hg) although it might not commence until higher pressures were attained.

3. In both the inverted and everted anastomoses occasional small abscesses and hematomas in the adjacent mesentery were noted. The number of each was equal in the two experiments. In each of the experiments, two animals had perianastomotic abscesses and three had small hematomas.

DISCUSSION

All anastomoses were performed 15 cm. proximal to the ileo-caecal valve in order to obviate two main causes of anastomotic breakdown, i.e. tension and inadequate blood supply. The importance of avoiding these well nigh catastrophic conditions has been emphasized by Halsted,[9] Getzen[47] and innumerable others. Anastomosis at this location in the ileum allows for no longitudinal distracting forces on the suture line and resection of a one to two centimetre segment allows a major branch of the superior mesenteric artery to enter the bowel in close proximity to the ends to be anastomosed. Moreover, resection of so small a segment should not lead to nutritional deficiency. Differences in the anastomoses with adhesions intact or removed or in inverted or everted anastomoses, therefore, tend to be due mainly to the presence or absence of adhesions, or the particular technique of anastomotic construction.

The shape of the healing curves in both experiments is not unexpected. Similarly shaped curves for the healing of bowel have been described by Cronin et al.[24] in the colon (rat), Fellows et al.[15] in the jejunum (dog), Herman et al.[16] in the colon (rat), Hamilton[95] in the ileum (dog), Mellish[94] in the ileum (rat), and Getzen et al.[91] in both the small intestine and colon (dog). That the anastomosis has appreciable bursting strength at six hours postoperatively, may be attributed to the sutures inserted at the time of operation as well as the deposition of fibrin between the opposed ends of bowel. Although this deposition of fibrin aids in sealing the anastomosis, Fellows et al.[15] have presented convincing data that most of the tensile strength of the anastomosis at this stage of the healing process is due to the sutures. However, the

gain in strength of the anastomosis between six and twelve hours is probably attributable to an increasing deposition of fibrin in the anastomotic cleft.

After twelve hours postoperatively, the strength of all anastomoses declined, reaching a minimum at three days in the inverted groups and at two days in the everted groups. Most investigators of intestinal healing would agree that the fall in strength seen at this interval of time is due to increasing inflammation, edema, hemorrhage and necrosis in the area of the anastomosis. The histological sections of the everted anastomosis support this contention. That this lag or substrate phase of the healing process persists slightly longer in the inverted anastomosis is consistent with the histological studies of Ravitch et al.[51] and Getzen et al.[91] noting more edema and inflammation in inverting closures. However, in the absence of histological sections of inverted anastomoses, this point remains conjectural in this study. Moreover, Hamilton[95] noted no difference in the healing of inverted and everted anastomoses and Gill et al.[97] noted more inflammation and increased microabscesses following everted closure. Loeb[96] also noted increased microabscesses with the everted technique.

The slight increase in strength of the anastomoses seen from two to four days is in all likelihood due to subsistence of inflammmation and edema. The rapid gain in tensile strength from four to ten days represents the phase of production and polymerization of collagen. This phase appears to be tapering off at ten days.

As may be noted from Figures 3 and 9, both inverted and everted anastomoses as well as anastomoses with adhesions left intact or removed by sharp dissection followed a similar pattern. With the

exception of the three day interval at which time the intact everted anastomoses were significantly stronger ($p<0.05$), there was no statistically significant difference in the strengths of intact inverted or everted anastomoses. The intact inverted anastomoses were stronger at the six hour, 12 hour, two day, five day, eight day, and 10 day intervals and the intact everted were stronger at 24 hours, three days, four days, and six days. In those anastomoses with adhesions removed by dissection, the inverted were stronger at the six hour, 24 hour, two day, four day, five day, eight day and 10 day intervals, while the everted were stronger at the 12 hour, three day, and six day intervals. Apart from the five day interval, at which time the inverted anastomoses were significantly stronger ($p<0.05$), these differences are again statistically insignificant.

It was concluded therefore, that neither inverted or everted anastomosis has an appreciable advantage over the other as regards gain in tensile strength in the first 10 days following operation. This conclusion, however, is at variance with most previously recorded data, only Hamilton[95] and Mellish[94] reporting no appreciable difference in the tensile strength of the two types of anastomoses. Loeb[96] reported that the inverted was significantly stronger at the third and seventh days after surgery, while Trueblood et al.,[26] Moretz[100] and Cohn[101] all reported that the inverting anastomosis was stronger throughout the healing period. On the other hand, Ravitch et al.[51] and Getzen et al.[91] reported that the everted anastomoses were significantly stronger in the early stages of the healing process.

The most significant result of these experiments, however, is the

demonstration that adhesions contribute significantly to the overall strength of the healing anastomoses early in the healing period. In the everted anastomoses adhesions contributed 32% to 68% of the overall strength of the anastomosis in the one to five day interval postoperatively. In the same postoperative interval, adhesions contributed 46% to 79% of the overall strength of everted anastomosis (Fig. 4 and 10). No similar data has been published previously.

Benjamin Travers[4] in 1812 was probably the first great exponent of the value of agglutinated peritoneal surfaces. Jobert[6] and Lembert[5] further emphasized the protective role of agglutinated peritoneal surfaces and described an inverting closure to optimize this agglutinating effect. For more than 100 years to follow, surgeons adopted various techniques of inverting closure to assure adequate intestinal healing. More recently with publications emphasizing the values of the everted anastomosis,[51,91] several investigators[26,97] have suggested that the everted anastomosis relies solely upon adhesions for adequate sealing of the suture line. Ravitch and co-workers,[51] in an attempt to disprove this hypothesis, wrapped anastomoses constructed by a variety of techniques with silastic gauze. Most of their anastomoses broke down. They concluded, therefore, that most anastomoses, no matter what the technique of construction, rely heavily on the formation of adhesions to assure successful healing. Cohn[101] also reported disruption of both inverted and everted anastomoses when wrapped with silastic. Pilot projects performed prior to beginning this study also suggest a heavy reliance of anastomoses on surrounding adhesions. Eight rats (four with an inverting anastomosis and four with an everting anastomosis) had the

anastomosis implanted in the subcutaneous tissue of the anterior abdominal wall. Seven rats died within four days or less and all these had leakage from the anastomosis and no adhesions surrounding the anastomosis. One rat survived and appeared well 10 days postoperatively when sacrificed. This anastomosis appeared intact and had adhesions surrounding half its circumference. A further eight rats (four with inverting anastomosis and four with everting anastomosis) had the anastomoses wrapped in sotra-tulle* and exteriorized on the anterior abdominal wall. All anastomoses leaked, none had adhesions surrounding them, and all animals died within 72 hours of operation. It would appear then that both inverting and everting anastomoses are equally dependent on adhesions for successful healing. The percentage contribution of adhesions to the overall strength of the anastomosis is similar for both inverting and everting anastomoses and, significantly, the maximal contribution occurs at the identical time interval, one to five days postoperatively, when the anastomosis itself is weakest and least able to withstand pressure distension.

Adhesions do not appear to be a major cause of intestinal obstruction, in the time period under study. Only one case of obstruction in both experiments could be attributed directly to the presence of adhesions. This animal (everting anastomosis) died of complete bowel obstruction following torsion of a loop of ileum around an adhesion. As previously described, the number of adhesions surrounding the anastomosis in no way correlated with the degree of obstruction, if any, proximal to anastomosis. Adhesions at this period

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*Roussel (Canada) Ltd., Montreal, Quebec.

of the healing process do not appear then, to be a prominent cause of intestinal obstruction following either inverting or everting anastomosis. The degree of obstruction at this stage appears to be directly related to the diameter of the lumen at the anastomosis which, in turn, predominantly governed by the degree of edema and inflammation and subsequent swelling at the suture line. This is not to say, however, that adhesions are not a significant factor in intestinal obstruction following abdominal surgery. Numerous authors[102,103,104] have stressed the importance of adhesions as a cause of intestinal obstruction. It is merely stated that adhesions do not appear to be a major cause of such in the first ten days following small-bowel anastomosis. That persistent adhesions may later lead to obstruction is not denied.

With regard to the influence of proximal obstruction on the healing process, our results are somewhat at variance with previous investigators. The work of Sako and Wangensteen[84] suggests that obstruction proximal to a healing intestinal anastomosis retards the healing of that anastomosis. The present data, however, suggests that slight obstruction proximal to the anastomosis has no effect on the healing process. Moderate proximal obstruction apparently retards the healing process, but in the everted group the number of animals is small (one). The marked proximal obstruction present in some animals with inverting anastomosis apparently did not retard the healing process although the number of animals is again small. Although these results are different from the results of previous investigators, the degree of obstruction present in these previous reports was usually total, while no animal in our experiment had total obstruction.

It was found, however, that the inverting closure led to significantly more obstruction at the site of the anastomosis than the everting closure. The obstruction was apparently due to edema and inflammation of the inturned flange with subsequent luminal stenosis. This observation is in agreement with those of Ravitch et al.,[51] Getzen et al.[91] and Gill et al.[97] although only Getzen records an incidence of obstruction similar to that found in this study. On the other hand, Hamilton,[95] and Healey et al.[89] note little difference in the number of cases of obstruction caused by these two types of closure. Only Dennis[105] records stenosis with an everting closure. This work was done in suckling pigs and the everting anastomosis apparently failed to grow with the animal, leading to late stomal stenosis. He does not mention if the suture was interrupted or continuous.

The overall mortality was somewhat greater in the group with inverting anastomoses (inverting 13.33%; everting 4.82%). Most animals dying following inverting anastomosis did so because of bowel obstruction secondary to luminal stenosis or occlusion. The predominant cause of death following everting closure was anastomotic leakage with generalized peritonitis. Getzen[47] Hamilton,[95] Gill et al.[97] Trueblood et al.[26] and Healey et al.,[89] all record no appreciable difference in mortality following inverting and everting anastomosis.

Apart from the high incidence of proximal obstruction seen in the animals with inverting closures, there appeared to be no difference in morbidity between the animals in Experiment #1 and Experiment #2. Several animals in each experiment had small abscesses or hematomas adjacent to the anastomosis.

As previously reported by Ravitch et al.,[51] Getzen and co-workers,[91] Hamilton,[95] Mellish,[94] and Hertzler and Tuttle,[88] the everting anastomosis was much simpler and quicker to construct than the inverting anastomosis. The visualization of submucosa was excellent and the angulation of vessels and turning in of the mesentery was certainly less in the everting closure.

The everting anstomosis was followed by a somewhat greater incidence of adhesions. This observation is in agreement with the majority of prior observations. Bichat,[3] however, noted more numerous adhesions with serosa-to-serosa contact rather than with mucosa-to-mucosa contact. Hertzler and Tuttle[88] and Getzen and co-workers[91] found no increase in adhesions with everting closures. Ravitch and co-workers,[51] Gill et al.,[97] Trueblood et al.,[26] Healey et al.,[89] Loeb,[96] Hamilton,[95] and Mellish,[94] all noted more adhesions surrounding everting closures than was the case with inverting closures. The difference in quantity and quality of adhesions in these two experiments was, however, minimal. Further findings are in contradistinction to the findings of Trueblood et al.,[26] in that adhesions did not seem to be a sine qua non for effective sealing of the everting anastomosis, they could be effectively removed without opening the bowel, no fistulae were noted under adhesions covering everting closures, and the incidence of perianastomotic abscesses covered by adhesions was no greater following everting closure. All groups reported here had a higher incidence of adhesions than reported by Cronin, Jackson and Dunphy.[24]

Sections of the everting anastomosis did not appear to differ

markedly from the pattern of intestinal healing found by previous investigators. In particular, the healing of these everted anastomosis appeared to follow a pattern similar to that described by Getzen and co-workers[91] and Ravitch et al.[51] However, contrary to the observations of Getzen et al.,[91] serosa cell proliferation did not cover the fibrin seal within 24 hours, this process being delayed until three to 10 days in this experiment. Also, contrary to the observations of Ravitch et al.,[51] mucosal continuity was not noted at 72 hours, but usually delayed until the eighth or tenth postoperative day. Our observations are in direct agreement with those of Getzen et al.[91] that everting anastomosis does not lead to an extremely intense polymorphonuclear infiltration, does not cause mucocoele formation, does not lead to formation of cysts containing sebum-like material, and is only infrequently associated with microabscess formation and microfistualization. These findings are in direct contrast to those of Gill et al.[97] Also in agreement with Getzen et al.[91] and in contrast with Gill et al.,[97] is the observation that the everted mucosa did not remain viable, most of it sloughing within the ten day observation period.

After examining inverted closures from another project, it was concluded that no significant histological difference in the healing of inverting and everting anastomoses could be ascertained. This was also noted by Hertzler and Tuttle[88] and Ravitch et al.[51] Getzen and co-workers[91] believe the histological appearance of everting anastomoses to be superior, while Gill et al.[97] and Trueblood et al.[26] believe that the inverting anastomosis has a superior histological appearance. The histological appearance of collagen on the fifth postoperative day

coincides with the data of Letwin and Williams,[60] who also worked in this laboratory.

In general, however, the overall healing of the anastomosis followed the descriptions of Herman et al.,[16] Fellows et al.,[15] Dennis,[20,21] Flint,[17] Grey,[106] Lee,[52] Mall,[107] Sabin,[28] Poth,[57] and Martzloff and Suckow.[30,31]

In short, the histological findings support the dictum of Benjamin Travers.[4]

"The union of a divided bowel requires the contact of the cut extremities in their entire circumference. ... The species of suture employed is of secondary importance if it secures this contact."

The hydroxyproline concentrations follow a pattern similar to, but not identical with, the curves of Cronin, Jackson and Dunphy,[24] and Olsen, Letwin and Williams.[18] The curve of Cronin et al. represents the percentage of collagen in the bowel wound and this parameter they found to decrease from wounding till three days postoperatively, followed by a rapid increase to 10 days, with a subsequent slight decrease from 10 to 14 days. Olsen et al. report minimal diminution in the hydroxyproline content of one and two layer anastomosis from the time of wounding until the third postoperative day, when the hydroxyproline began to increase rapidly and continued to do so until termination of their study at five days.

As regards the curve in Fig. 8, the fall in hydroxyproline concentration from 24 hours to three days is attributed to collagen breakdown in the demolition and substrate phase of healing. The gradual but erratic rise thereafter, represents the continuing synthesis of collagen

in the wound as well as in the adjacent bowel. No satisfactory explanation is apparent for the changes in the hydroxyproline content in the first 24 hours after wounding, as well as the dip in the curve between six and 10 days.

As regards methodology, this work may be criticized from two points of view. In the first instance, we have measured only the bursting pressure of the segment of bowel. In order to assess exactly the strength of the anastomosis, the tension exerted on the anastomosis at the time of rupture should be calculated. By modifying the law of LaPlace:

$$T = \frac{P}{\frac{1}{R_1} + \frac{1}{R_2}}$$

where T = tension
P = pressure
R_1 = radius at time T_1
R_2 = radius at time T_2

to apply to a cylinder, the following equations may be derived:

$$T_{(long)} \text{ (longitudinal wall tension)} = \frac{PR}{2}$$

$$T_{(circ)} \text{ (circular wall tension)} = PR$$

In order then to calculate the circular wall tension (which is the force responsible for anastomotic disruption) at the time of rupture, it is necessary to measure the radius of curvature of the bowel at the anastomosis at the moment of disruption. The product of pressure and radius then gives the circular wall tension at the time of rupture. As Nelson and Anders[25] have pointed out, the circular tension exerted on the anastomosis itself if often far less than the circular tension exerted on adjacent bowel because of inflammation, edema, sutures present, fibrosis and inversion of tissue, reducing not only the radius of curvature at the anastomosis, but also the capacity of this segment to

expand. This accounts not only for rupture of the bowel at a point other than the anastomosis in eight and ten day specimens, but also may lead to somewhat erroneous concepts as to the overall strength of the anastomosis at an earlier time.

In the absence of an apparatus to definitively measure the radius of the anastomosis at the time of rupture, a crude control of this parameter was employed using visual inspection of the anastomoses. Any anastomoses in which the radius appeared significantly greater or less than what appeared to be an average for the entire experiment were rejected from the study. In this way the radius was maintained relatively constant, and the bursting pressure, though not an exact measure of bursting strength, would vary directly with it. These experiments then fall into the trap of most investigators in this field. Although the bursting strength data would be subject to some change if bursting tensions were calculated rather than using bursting pressures, the trends would remain constant as an effort was made to keep the radius constant. In the future it is hoped that an apparatus consisting of a pressure transducer, Gilson recorder* and a camera triggered by pressure drop in the transducer will allow simultaneous measurement of pressure and radius and thereby facilitate exact calculation of the bursting strength.

A second criticism which may be levelled at this work is the manner in which adhesions were removed from the anastomoses. It may be argued that either too little or too much tissue was removed, thus either increasing or decreasing the true strength of the anastomosis. Sharp dissection was used throughout removal of adhesions to minimize

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* Gilson Medical Electronics, Middleton, Wisconsin.

tearing and distortion of tissues. However, most adhesions up to the three to five day interval were easily removable by blunt dissection. In the early period of the healing process it may be thought that removing adhesions could easily tear the edematous, inflamed and fragile tissue. However, in both experiments, those anastomoses in which adhesions were removed were stronger at six hours and 12 hours postoperatively than those left intact. Although at a loss to explain this phenomenon, it is suggested that this indicates a degree of care taken in removal of adhesions. Later in the healing process (one to five days), when the most significant results were obtained, I was confident that adhesions could be effectively and totally removed without damaging the underlying anastomosis. By the six day, eight day and 10 day intervals, the adhesions had become quite firmly adherent to the underlying bowel and this union had, in addition, become increasingly more fibrous in nature. In dissection of these adhesions, great care was taken to assure the integrity of the bowel wound itself. Consequently, fibrous portions of adhesions may have been left adherent to the bowel wound. If this were indeed the case, the bursting pressures of those anastomoses in which the adhesions had been removed would be expected to be less than recorded. In answer to this second criticism, then, it can only be stressed that extreme care was taken in removal of adhesions.

Regarding the contribution of adhesions to the overall tensile strength of intestinal anastomosis, this is a function long suspected, convincingly proven by Ravitch et al.,[51] but, to my knowledge, never quantitatively demonstrated. Poth[57] has stated "The mass of edematous tissue surrounding an essentially poor repair may support the tissues and splint them to such a degree that a considerable pressure is required

to disrupt the site of the suture. If this edematous tissue is meticulously dissected away, the anastomosis in such an instance will practically fall apart and withstand no intraluminal pressure whatsoever". Adhesions appear to act in a somewhat analogous manner. This is not to say that adhesions are necessarily the sequelae of faulty anastomotic construction, but rather that they form an additional barrier protecting the anastomosis in the first few days following its construction when, no matter what technique of construction is used, the strength of the bowel wound itself is at a minimum. Neither is it advocated that this represents the sole function of adhesions. Myllärniemi and Karppinen[48] and Ellis[46] have presented convincing evidence that adhesions act as vascular grafts to ischemic areas of intestine which are undoubtedly present to some degree in most anastomoses. Adhesions act further to seal off areas of leakage, thus indirectly adding to tensile strength of the anastomosis. The splinting function of adhesions demonstrated in this study is added to these other functions.

In addition, this splinting function of adhesions is not proposed as a teleological explanation of adhesion formation. Ischemia intestinal leakage, inflammation and sutures undoubtedly are factors stimulating adhesion formation. Although peritoneal trauma and denudation have been proposed as a factor stimulating adhesion formation, there is a great deal of evidence suggesting that this concept is erroneous.

No matter what the factor stimulating the formation of the adhesions, they do splint and protect the anastomosis. In the light of this knowledge, perhaps present trends of attempting to prevent adhesions

around intestinal suture lines should be more closely examined. Corticosteroids (e.g. dexamethazone - Watts et al.[108]) not only may prevent adhesions but also retard the healing process in the bowel itself. Theoretically at least, such therapy removes a large portion of the margin of safety of intestinal healing. Isolating the anastomosis is obviously not the answer. The use of heparin to prevent adhesions may be followed by coagulationopathies and most chemicals used to prevent adhesions are far from uniformly successful. Perhaps for the moment, the presence of adhesions following anastomosis should be gratefully accepted and their later unwanted sequelae treated as they occur.

SUMMARY AND CONCLUSIONS

1. Adhesions form in great numbers around both inverted and everted anastomoses in the ileum of the rat. These adhesions appear early in the postoperative period and are still prevalent 10 days postoperatively. No significant difference in the number of adhesions surrounding either inverted or everted anastomoses was noted, although the number was slightly greater around the everted closures.

2. In the inverted anastomoses, the strength of the ileal wound increased from six to 12 hours postoperatively, then declined, reaching a minimum at three days. The strength then increased progressively until 10 days. The everted anastomoses followed a similar pattern except that they reached a minimum strength at two days postoperatively. This pattern was followed whether the anastomosis was left intact or whether the adhesions were dissected from it. No convincing evidence was found that either type of anastomosis was significantly stronger then the other whether intact or with adhesions removed.

3. Following either inverted or everted anastomosis, various degrees of obstruction proximal to the anastomosis were noted. However, both the number of animals with proximal obstruction, as well as the extent of the obstruction, were far greater in those animals with inverted anastomoses than in those with everted anastomoses. This suggests that everted anastomosis may be the procedure of choice in small children where the bowel lumen is narrow.

4. The presence of, or extent of, obstruction proximal to the anastomosis appeared in no way related to the number of adhesions surrounding the anastomosis. This was true for both inverted and

everted anastomoses. That adhesions may lead to later bowel obstruction (torsion, kinking, compression), cannot be denied. They do not, however, appear to be a significant cause of intestinal obstruction in the time interval studied.

5. With the possible exception of animals with a moderate degree of obstruction proximal to the anastomosis, the presence of, or degree of, obstruction proximal to the anastomosis did not appear to significantly alter the strength of the anastomosis. This was again true for both the inverted and everted anastomosis.

6. Histological examination of the everted anastomoses did not disclose any difference in those anastomoses left intact or those from which adhesions had been dissected, apart from the presence or absence of adhesions. Of some interest was the significant amount of collagen identified histologically in the adhesions surrounding the anastomosis.

7. The hydroxyproline concentrations of the inverted anastomoses followed a pattern somewhat similar to the bursting pressures with an initial rise from six to 24 hours, falling off from 24 hours to three days, gradual increase from three to six days, moderate decrease from six to eight days and then a moderate increase from eight to ten days.

The minimal difference in hydroxyproline concentrations in intact anastomoses and in those from which adhesions had been removed, is at variance with the conclusions derived histologically from everted anastomoses regarding the prevalence of collagen in the surrounding adhesions. This contradiction is to be examined more completely in subsequent experiments.

8. The occasional stripping of adhesions noted with pressure distension of the ileal segments suggested that a similar factor may be operative in vivo. Postoperative ileus and distension may also lead to stripping of adhesions from the anastomosis. If this phenomenon occurs at a critical time and in a critical area of the anastomosis, the sequel could well be anastomotic disruption with subsequent abscess formation and/or generalized peritonitis.

9. The data concerning the presence or absence of adhesions is somewhat conflicting. With inverted anastomosis, significantly more animals with adhesions incompletely surrounding the anastomosis had a bursting pressure greater than the mean of their group than was found in either the total group or in those with adhesions completely surrounding the anastomosis. This may imply that the absence of adhesions around an inverted anastomosis suggests an integrally strong bowel wound. With everted anastomoses, however, quite the reverse was found. Those animals with anastomoses incompletely surrounded by adhesions had a much higher percentage of cases in which the bursting pressure was less than the mean of their group, than was found in the total group or the group with adhesions completely surrounding the anastomosis. This suggests that absence of adhesions may, in fact, weaken the everted anastomosis. However, statistical analysis of bursting pressures in both Experiment #1 and Experiment #2 supports neither of these contentions.

10. Adhesions contribute little, if any, to the tensile strength of the anstomosis in the first 24 hours following surgery. However, from 24 hours to 10 days postoperatively, adhesions do contribute to

the ability of the anastomosis to withstand pressure distension. Significantly, this contribution is greatest in the period from one to five days postoperatively when the anastomosis itself is weakest and least able to withstand this pressure distension. This is equally true of both inverted and everted anastomoses.

It is suggested, therefore, that intestinal anastomoses in clinical practice be allowed intimate contact with surrounding viscera and peritoneal surfaces. Factors diminishing this contact such as drains, fluid, and hematomas may prevent the immediate formation of adhesions which in turn may lead to anastomotic disruption. Similarly, drugs which allegedly prevent or decrease the number of adhesions (heparin, hyaluronidase, streptokinase, detergents, etc.) should only be used with caution following intraperitoneal anastomosis of the gastro-intestinal tract.

TABLES

TABLE I

INVERTED ANASTOMOSIS

Time of Sacrifice	Mean Bursting Pressure Anastomosis Intact	Anastomosis With Adhesions Removed	p value
6 hours	73.5 ± 27.4	102 ± 14.1	0.05 - 0.10
12 hours	110 ± 25.3	119 ± 10.1	0.25 - 0.30
24 hours	70.0 ± 5.89	47.5 ± 14.7	0.010 - 0.025
2 days	53.0 ± 15.1	17.5 ± 12.6	0.005 - 0.010
3 days	38.0 ± 5.41	13.3 ± 14.5	0.005 - 0.010
4 days	66.5 ± 9.71	21.5 ± 11.8	< 0.005
5 days	188 ± 37.1	94.0 ± 29.6	0.005 - 0.010
6 days	188.5 ± 25.0	147.5 ± 61.1	0.10 - 0.15
8 days	273.5 ± 29.0	256 ± 33.6	0.20 - 0.25
10 days	308 ± 35.8	304.5 ± 48.2	> 0.45

TABLE II

INVERTED ANASTOMOSIS - CORRELATION OF PROXIMAL OBSTRUCTION AND ADHESIONS

TOTAL GROUP OF ANIMALS WITH INVERTED ANASTOMOSES (78)

Animals with no proxiaml obstruction	(20)	26%
Animals with slight proximal	(32)	41%
Animals with moderate proximal obstruction	(18)	23%
Animals with marked proximal obstruction	(8)	10%

ANIMALS WITH INVERTED ANASTOMOSES AND ADHESIONS SURROUNDING THE ENTIRE CIRCUMFERENCE OF THE ANASTOMOSIS (60)

Animals with no proximal obstruction	(16)	27%
Animals with slight proximal obstruction	(24)	40%
Animals with moderate proximal obstruction	(15)	25%
Animals with marked proximal obstruction	(5)	8%

ANIMALS WITH INVERTED ANASTOMOSIS AND ADHESIONS INCOMPLETELY SURROUNDING THE ANASTOMOSIS (18)

Animals with no proximal obstruction	(4)	22%
Animals with slight proximal obstruction	(8)	44%
Animals with moderate proximal obstruction	(3)	17%
Animals with marked proximal obstruction	(3)	17%

TABLE III

INVERTED ANASTOMOSIS - CORRELATION OF ADHESIONS AND PROXIMAL OBSTRUCTION

IN THE TOTAL GROUP OF ANIMALS WITH INVERTED ANASTOMOSES (78)

(60)	77%	Had adhesions completely surrounding the anastomosis
(18)	23%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH NO PROXIMAL OBSTRUCTION (20)

(17)	85%	Had adhesions completely surrounding the anastomosis
(3)	15%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH SLIGHT PROXIMAL OBSTRUCTION (32)

(23)	72%	Had adhesions completely surrounding the anastomosis
(9)	28%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH MODERATE PROXIMAL OBSTRUCTION (18)

(15)	83%	Had adhesions completely surrounding the anastomosis
(3)	17%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH MARKED PROXIMAL OBSTRUCTION (8)

(5)	62.5%	Had adhesions completely surrounding the anastomosis
(3)	37.5%	Had adhesions incompletely surrounding the anastomosis

TABLE IV

MEAN WEIGHT OF ANIMALS (IN GRAMS) IN EXPERIMENT # 1

	Anastomosis Intact	Anastomosis With Adhesions Removed
On arrival	280 ± 8.97	279 ± 10.1
At operation	324 ± 22.7	319 ± 28.4
At sacrifice	328 ± 23.6	323 ± 27.3

MEAN WEIGHT OF ANIMALS (IN GRAMS) IN EXPERIMENT # 2

	Anastomosis Intact	Anastomosis With Adhesions Removed
On arrival	289 ± 15.8	283 ± 16.4
At operation	310 ± 21.1	308 ± 17.6
At sacrifice	324 ± 18.5	321 ± 12.3

TABLE V

MEAN HYDROXYPROLINE CONTENT OF INVERTED ANASTOMOSES

(in milligrams/gram frozen weight of tissue)

Time of Sacrifice	Anastomosis Intact	Anastomosis With Adhesions Removed	p Values
6 hours	0.84 ± 0.46	1.16 ± 0.10	0.1 - 0.15
12 hours	0.94 ± 0.17	0.89 ± 0.05	0.3 - 0.35
24 hours	1.22 ± 0.18	1.30 ± 0.24	0.3 - 0.35
2 days	0.88 ± 0.11	0.90 ± 0.12	0.1 - 0.15
3 days	0.71 ± 0.41	0.69 ± 0.09	>0.45
4 days	0.80 ± 0.17	0.80 ± 0.06	>0.45
5 days	0.86 ± 0.12	0.88 ± 0.10	0.4 - 0.45
6 days	1.32 ± 0.27	1.97 ± 0.59	0.025 - 0.05
8 days	1.00 ± 0.15	1.16 ± 0.08	0.05 - 0.1
10 days	1.24 ± 0.12	1.47 ± 0.22	0.05 - 0.1

TABLE VI

EVERTED ANASTOMOSIS

	Mean Bursting Pressure		
Time of Sacrifice	Anastomosis Intact	Anastomosis With Adhesions Removed	p value
6 hours	47.5 ± 38.6	73.8 ± 33.5	0.15 - 0.20
12 hours	106 ± 34.5	130 ± 43.8	0.20 - 0.25
24 hours	76.3 ± 19.7	41.3 ± 23.9	0.025 - 0.05
2 days	37.0 ± 10.1	8.50 ± 8.70	< 0.005
3 days	60.0 ± 11.6	27.5 ± 11.9	< 0.005
4 days	87.5 ± 46.6	18.8 ± 14.4	0.01 - 0.025
5 days	155 ± 37.0	34.8 ± 35.1	< 0.005
6 days	212 ± 45.7	187.5 ± 92.2	0.30 - 0.35
8 days	247.5 ± 41.1	202.5 ± 86.6	0.15 - 0.20
10 days	300 ± 37.4	263 ± 23.1	0.15 - 0.20

TABLE VII

EVERTED ANASTOMOSIS - CORRELATION OF PROXIMAL OBSTRUCTION AND ADHESIONS

TOTAL GROUP OF ANIMALS WITH EVERTED ANASTOMOSES (79)

Animals with no proximal obstruction	(68)	86%
Animals with slight proximal obstruction	(10)	13%
Animals with moderate proximal obstruction	(1)	1%

ANIMALS WITH EVERTED ANASTOMOSES AND ADHESIONS SURROUNDING THE ENTIRE CIRCUMFERENCE OF THE ANASTOMOSIS (68)

Animals with no proximal obstruction	(60)	88%
Animals with slight proximal obstruction	(7)	10%
Animals with moderate proximal obstruction	(1)	1%

ANIMALS WITH EVERTED ANASTOMOSES AND ADHESIONS INCOMPLETELY SURROUNDING THE ANASTOMOSIS (11)

Animals with no proximal obstruction	(8)	73%
Animals with slight proximal obstruction	(3)	27%

TABLE VIII

EVERTED ANASTOMOSIS - CORRELATION OF ADHESIONS AND PROXIMAL OBSTRUCTION

IN THE TOTAL GROUP OF ANIMALS WITH EVERTED ANASTOMOSES (79)

(68)	86%	Had adhesions completely surrounding the anastomosis
(11)	14%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH NO PROXIMAL OBSTRUCTION (68)

(60)	88%	Had adhesions completely surrounding the anastomosis
(8)	12%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH SLIGHT PROXIMAL OBSTRUCTION (10)

(7)	70%	Had adhesions completely surrounding the anastomosis
(3)	30%	Had adhesions incompletely surrounding the anastomosis

IN THE ANIMALS WITH MODERATE PROXIMAL OBSTRUCTION (1)

(1)	100%	Had adhesions completely surrounding the anastomosis

TABLE IX

COMPARISON OF BURSTING PRESSURES - INVERTED AND EVERTED ANASTOMOSES

Time of Sacrifice	Anastomoses Intact	Anastomoses With Adhesions Removed
6 hours	Inverted stronger p 0.15 - 0.20	Inverted stronger p 0.05 - 0.10
12 hours	Inverted stronger p 0.40 - 0.45	Everted stronger p 0.30 - 0.35
24 hours	Everted stronger p 0.25 - 0.30	Inverted stronger p 0.30 - 0.35
2 days	Inverted stronger p 0.05 - 0.10	Inverted stronger p 0.10 - 0.15
3 days	Everted stronger p 0.005 - 0.01	Everted stronger p 0.10 - 0.15
4 days	Everted stronger p 0.20 - 0.25	Inverted stronger p 0.35 - 0.40
5 days	Inverted stronger p 0.10 - 0.15	Inverted stronger p 0.025 - 0.05
6 days	Everted stronger p 0.15 - 0.20	Everted stronger p 0.20 - 0.25
8 days	Inverted stronger p 0.15 - 0.20	Inverted stronger p 0.10 - 0.15
10 days	Inverted stronger p 0.10 - 0.15	Inverted stronger p 0.10 - 0.15

APPENDIX

INVERTED ANASTOMOSIS - SACRIFICED AT SIX HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesions
		arrival	operation	sacrifice				
1	intact	275	324	324	94	marked	5/8	fat pad¶
2	intact	290	340	340	36	none	entire	fat pad
3	intact	285	338	338	94	slight	1/3	fat pad
4	intact	280	282	282	70	moderate	1/2	fat pad
5	adhesions removed	280	316	316	112	slight	entire	fat pad
6	adhesions removed	295	330	330	112	moderate	1/4	fat pad
7	adhesions removed	285	300	300	82	slight	1/3	fat pad
8	adhesions removed	285	296	296	102	marked	1/2	fat pad

* Circumference of anastomosis covered by adhesions

¶ Fat Pad - The testicular fat pad. The processus vaginalis of the rat remains widely patent allowing the fat pad direct communication with the peritoneal cavity. This amorphous mass of fatty and areolar tissue seems to function much like the human omentum.

INVERTED ANASTOMOSES - SACRIFICED AT 12 HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesions
		arrival	operation	sacrifice				
1	intact	290	335	335	94	moderate	entire	fat pad & small bowel
2	intact	280	325	322	142	moderate	entire	fat pad & small bowel
3	intact	275	338	338	118	moderate	entire	fat pad & small bowel
4	intact	280	320	322	86	moderate	entire	fat pad, small bowel & mesentery
5	adhesions removed	285	355	360	116	marked	entire	fat pad & small bowel
6	adhesions removed	280	330	330	134	moderate	entire	fat pad, small bowel & stomach
7	adhesions removed	295	364	366	112	moderate	entire	fat pad & small bowel
8	adhesions removed	270	356	362	114	moderate	entire	fat pad & small bowel

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT 24 HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams arrival	operation	sacrifice	Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
1	intact	280	305	305	64	marked	entire	fat pad
2	intact	285	360	360	70	moderate	entire	fat pad
3	intact	280	320	320	78	marked	entire	fat pad & small bowel
4	intact	290	300	288	68	marked	entire	fat pad
5	adhesions removed	275	320	300	50	marked	entire	fat pad
6	adhesions removed	295	260	258	26	moderate	entire	fat pad & small bowel
7	adhesions removed	275	260	260	56	marked	1/8	fat pad
8	adhesions removed	280	318	316	58	moderate	entire	fat pad & small bowel

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT TWO DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
		arrival	operation	sacrifice				
1	intact	290	322	316	64	slight	entire	fat pad, small bowel & mesentery
2	intact	290	380	370	64	slight	entire	fat pad & small bowel
3	intact	280	350	340	32	slight	entire	fat pad & small bowel
4	intact	275	320	320	52	slight	entire	fat pad
5	adhesions removed	300	350	334	36	slight	entire	fat pad & small bowel
6	adhesions removed	275	360	330	8	slight	entire	fat pad & small bowel
7	adhesions removed	280	368	348	14	slight	1/2	fat pad
8	adhesions removed	280	320	316	12	slight	entire	fat pad

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT THREE DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams arrival	operation	sacrifice	Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
1	intact	285	320	306	30	moderate	entire	fat pad & small bowel
2	intact	270	300	278	40	none	entire	fat pad & small bowel
3	intact	285	350	345	42	none	3/4	fat pad
4	intact	285	324	332	40	none	entire	fat pad
5	adhesions removed	265	310	302	6	none	entire	fat pad
6	adhesions removed	280	300	302	30	slight	nil	————
7	adhesions removed	295	310	310	4	none	entire	fat pad & small bowel

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT FOUR DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
		arrival	operation	sacrifice				
1	intact	285	348	350	70	slight	entire	fat pad
2	intact	290	348	315	52	slight	entire	fat pad & small bowel
3	intact	260	318	316	72	slight	2/3	fat pad
4	intact	260	310	310	72	slight	entire	fat pad & small bowel
5	adhesions removed	275	280	275	10	slight	2/3	fat pad & small bowel
6	adhesions removed	270	320	320	14	slight	entire	fat pad & small bowel
7	adhesions removed	265	340	340	26	slight	entire	fat pad & small bowel
8	adhesions removed	280	310	355	36	moderate	entire	fat pad & small bowel

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT FIVE DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams arrival	operation	sacrifice	Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
1	intact	300	360	375	165	slight	entire	fat pad
2	intact	270	350	360	208	slight	entire	fat pad
3	intact	280	330	342	230	slight	entire	fat pad & small bowel
4	intact	285	320	325	150	slight	entire	fat pad
5	adhesions removed	295	330	335	74	none	entire	fat pad
6	adhesions removed	262	320	335	80	moderate	entire	fat pad & small bowel
7	adhesions removed	265	270	310	128	slight	entire	fat pad

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT SIX DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams arrival	operation	sacrifice	Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
1	intact	295	310	328	210	none	entire	fat pad
2	intact	270	300	320	164	slight	entire	fat pad
3	intact	275	290	292	170	slight	entire	fat pad, small bowel & mesentery
4	intact	265	370	380	210	none	entire	fat pad & small bowel
5	adhesions removed	280	310	318	192	slight	entire	fat pad
6	adhesions removed	270	320	340	208	none	entire	fat pad & small bowel
7	adhesions removed	280	360	360	100	none	entire	fat pad
8	adhesions removed	275	370	380	90	slight	entire	fat pad

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT EIGHT DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
		arrival	operation	sacrifice				
1	intact	275	320	340	270	moderate	7/8	fat pad & small bowel
2	intact	275	320	318	298	none	entire	fat pad & small bowel
3	intact	280	302	318	292	slight	2/3	fat pad
4	intact	290	300	295	234	moderate	entire	fat pad
5	adhesions removed	280	290	300	206	none	entire	fat pad, small bowel & mesentery
6	adhesions removed	280	330	338	278	slight	3/4	fat pad & small bowel
7	adhesions removed	290	330	330	270	none	3/4	fat pad & small bowel
8	adhesions removed	275	300	320	270	none	entire	fat pad

* Circumference of anastomosis covered

INVERTED ANASTOMOSIS - SACRIFICED AT 10 DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*	Type of Adhesion
		arrival	operation	sacrifice				
1	intact	285	320	340	360	none	entire	fat pad
2	intact	285	300	322	290	none	entire	fat pad & small bowel
3	intact	270	310	340	280	moderate	entire	fat pad & small bowel
4	intact	275	295	340	302	slight	2/3	fat pad & small bowel
5	adhesions removed	280	300	322	300	none	entire	fat pad & small bowel
6	adhesions removed	295	300	318	370	none	1/4	fat pad
7	adhesions removed	280	305	300	294	none	entire	fat pad & small bowel
8	ahdesions removed	260	330	340	254	slight	entire	fat pad

* Circumference of anastomosis covered

HYDROXYPROLINE CONCENTRATIONS

(milligrams hydroxyproline/gram dry weight of tissue)

	TIME OF SACRIFICE									
Rat Number	6 hrs.	12 hrs.	24 hrs.	2 days	3 days	4 days	5 days	6 days	8 days	10 days
1	0.71	1.10	0.98	0.72	0.29	0.78	0.96	1.14	0.94	1.35
2	0.32	1.07	1.41	0.90	0.45	0.57	0.76	1.19	0.81	1.39
3	0.92	0.85	1.26	0.88	1.17	0.94	0.95	1.22	1.15	1.09
4	1.42	0.74	1.23	0.68	0.91	0.90	0.75	1.71	1.08	1.21
5	1.11	0.98	1.05	0.93	0.77	0.75	0.79	2.63	1.17	1.69
6	1.29	0.84	1.59	0.97	0.60	0.74	0.86	1.20	1.25	1.21
7	1.06	0.85	1.17	0.73	0.69	0.86	0.98	2.14	1.17	1.39
8	1.16	0.89	1.37	0.98		0.83		1.91	1.05	1.61

EVERTED ANASTOMOSIS - SACRIFICED AT SIX HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	290	330	330	90	slight	1/3
2	intact	280	325	325	70	none	1/8
3	intact	260	300	300	10	none	1/3
4	intact	290	300	300	20	none	entire
5	adhesions removed	260	340	340	100	none	entire
6	adhesions removed	290	300	300	65	none	nil
7	adhesions removed	300	330	330	100	none	1/3
8	adhesions removed	280	320	320	30	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT 12 HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	300	320	320	150	slight	entire
2	intact	270	320	325	90	none	entire
3	intact	280	335	340	70	none	entire
4	intact	270	365	370	115	none	entire
5	adhesions removed	270	305	315	160	slight	entire
6	adhesions removed	280	320	330	70	slight	1/2
7	adhesions removed	270	320	335	165	none	entire
8	adhesions removed	270	305	315	124	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT 24 HOURS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	260	340	350	70	moderate	entire
2	intact	290	320	325	70	none	3/4
3	intact	300	340	345	105	slight	entire
4	intact	300	300	315	60	none	2/3
5	adhesions removed	260	300	310	30	none	entire
6	adhesions removed	280	320	325	50	none	entire
7	adhesions removed	300	320	320	15	none	entire
8	adhesions removed	270	315	315	70	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT TWO DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions
		arrival	operation	sacrifice			
1	intact	300	310	330	30	none	entire
2	intact	310	340	335	28	none	entire
3	intact	300	300	295	50	none	entire
4	intact	270	335	320	40	none	entire
5	adhesions removed	300	325	330	20	none	entire
6	adhesions removed	300	320	335	4	none	entire
7	adhesions removed	270	295	305	10	none	entire
8	adhesions removed	270	305	315	0	none	2/3

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT THREE DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	290	350	360	70	none	entire
2	intact	300	330	340	70	none	entire
3	intact	280	300	320	50	none	2/3
4	intact	310	315	320	50	none	entire
5	adhesions removed	310	340	350	35	none	entire
6	adhesions removed	270	330	340	15	none	entire
7	adhesions removed	300	310	320	40	none	entire
8	adhesions removed	310	340	340	20	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT FOUR DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	290	320	360	90	none	entire
2	intact	320	300	320	150	none	entire
3	intact	300	320	340	70	none	entire
4	intact	310	300	320	40	none	entire
5	adhesions removed	270	300	330	40	none	entire
6	adhesions removed	300	310	320	15	none	entire
7	adhesions removed	290	310	330	10	none	entire
8	adhesions removed	300	320	325	10	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT FIVE DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	310	300	320	100	none	entire
2	intact	290	300	315	170	none	entire
3	intact	290	320	330	180	none	entire
4	intact	270	280	295	170	none	entire
5	adhesions removed	290	320	300	8	none	entire
6	adhesions removed	280	295	315	6	none	entire
7	adhesions removed	290	300	325	45	none	entire
8	adhesions removed	310	310	315	80	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT SIX DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	300	300	320	200	slight	entire
2	intact	300	290	320	270	none	entire
3	intact	290	310	320	220	none	entire
4	intact	290	300	320	160	slight	entire
5	adhesions removed	280	290	305	60	none	entire
6	adhesions removed	270	290	315	210	none	entire
7	adhesions removed	280	290	335	200	none	entire
8	adhesions removed	320	320	325	280	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT EIGHT DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	280	280	310	220	none	entire
2	intact	265	280	310	300	none	entire
3	intact	280	280	295	210	none	entire
4	intact	320	295	300	260	none	entire
5	adhesions removed	290	280	320	220	slight	entire
6	adhesions removed	260	270	305	300	none	entire
7	adhesions removed	260	295	320	200	none	entire
8	adhesions removed	270	270	300	90	none	entire

* Circumference of anastomosis covered

EVERTED ANASTOMOSIS - SACRIFICED AT 10 DAYS POSTOPERATIVELY

Rat Number	Anastomosis	Weight in grams			Bursting Pressure (mm. Hg)	Degree of Proximal Obstruction	Extent of Adhesions*
		arrival	operation	sacrifice			
1	intact	275	300	320	310	none	entire
2	intact	300	295	350	340	none	entire
3	intact	270	275	295	300	none	entire
4	intact	275	295	320	250	slight	7/8
5	adhesions removed	260	300	320	290	none	entire
6	adhesions removed	300	290	330	250	none	entire
7	adhesions removed	280	300	330	250	none	entire

* Circumference of anastomosis covered

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